```
=> d que
L18                 STR
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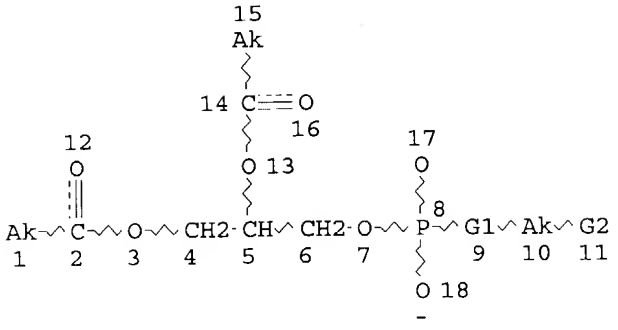

← zwitterion

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REP G1=(0-1) O
VAR G2=19/20/21
NODE ATTRIBUTES:
CHARGE  IS *-      AT  18
CHARGE  IS *+      AT  19
CHARGE  IS *+      AT  20
CHARGE  IS *+      AT  21
NSPEC   IS RC      AT  19
NSPEC   IS RC      AT  20
NSPEC   IS RC      AT  21
CONNECT IS E1  RC AT   1
CONNECT IS E2  RC AT  10
CONNECT IS E1  RC AT  15
CONNECT IS E1  RC AT  17
CONNECT IS E1  RC AT  18
DEFAULT MLEVEL IS ATOM
GGCAT   IS LIN  AT   1
GGCAT   IS SAT  AT  10
GGCAT   IS LIN  AT  15
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  21

STEREO ATTRIBUTES: NONE
L19         2335 SEA FILE=REGISTRY SSS FUL L18
L24                STR
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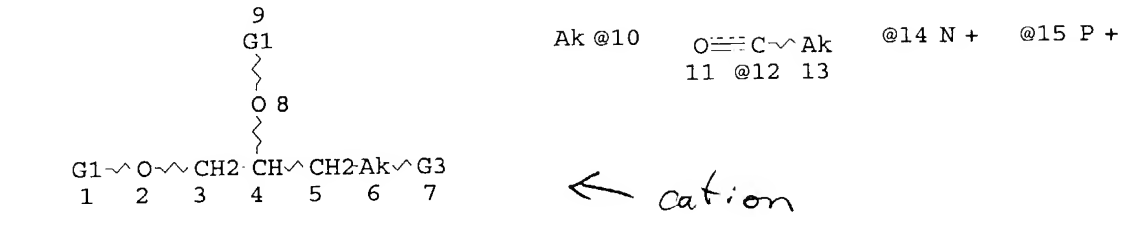


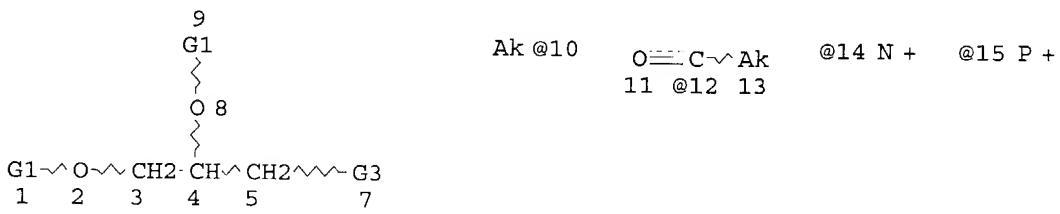
← cation

@16 S +

VAR G1=10/12
VAR G3=14/16/15
NODE ATTRIBUTES:
CHARGE IS *+ AT 14
CHARGE IS *+ AT 15
CHARGE IS *+ AT 16
NSPEC IS RC AT 14
NSPEC IS RC AT 15
NSPEC IS RC AT 16
CONNECT IS E2 RC AT 6
CONNECT IS E1 RC AT 10
CONNECT IS E1 RC AT 13
DEFAULT MLEVEL IS ATOM
GGCAT IS SAT AT 6
GGCAT IS LIN AT 10
GGCAT IS LIN AT 13
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
L26 STR



@16 S +

VAR G1=10/12
VAR G3=14/16/15
NODE ATTRIBUTES:
CHARGE IS *+ AT 14
CHARGE IS *+ AT 15
CHARGE IS *+ AT 16
NSPEC IS RC AT 14
NSPEC IS RC AT 15
NSPEC IS RC AT 16
CONNECT IS E1 RC AT 10
CONNECT IS E1 RC AT 13
DEFAULT MLEVEL IS ATOM
GGCAT IS LIN AT 10
GGCAT IS LIN AT 13
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

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STEREO ATTRIBUTES: NONE
L28          568 SEA FILE=REGISTRY SSS FUL L26
L31              SCR 2040
L34           15 SEA FILE=REGISTRY SSS FUL L31 AND L24
L35          583 SEA FILE=REGISTRY ABB=ON  PLU=ON  L28 OR L34
L38          187 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 AND L35
L40       228509 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIGENS+OLD,NT/CT
L41       301763 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DNA+OLD,NT/CT
L42       664086 SEA FILE=HCAPLUS ABB=ON  PLU=ON  NUCLEIC ACIDS+OLD,NT/CT
L43       170540 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DRUG DELIVERY SYSTEMS+OLD,NT/C
                 T
L44        14921 SEA FILE=HCAPLUS ABB=ON  PLU=ON  POLYNUCLEOTIDES+OLD,NT/CT
L45        39004 SEA FILE=HCAPLUS ABB=ON  PLU=ON  VACCINES+OLD,NT/CT
L47         2940 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "IMMUNIZATION (L) VACCINATION"
                 +OLD/CT
L49           13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 AND (L45 OR L47 OR
                 VACCIN? OR IMMUNIZ? OR IMMUNIS? OR DRUG DELIVERY SYSTEMS+OLD,NT
                 /CT(L)(VACCIN? OR IMMUNI? OR ORAL?))
L51           55 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 AND (L45 OR L47 OR
                 VACCIN? OR IMMUNI? OR L43) AND (L40 OR L41 OR L42 OR L44)
L52           59 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 OR L49


=> d l52 ibib ab hitind hitstr 1-59

L52  ANSWER 1 OF 59  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:466673  HCAPLUS
DOCUMENT NUMBER:          141:28640
TITLE:                    Liposomal glucocorticoids for use as antiinflammatory
                          agents
INVENTOR(S):              Panzner, Steffen; Braeuer, Rolf; Kinne, Raimund W.;
                          Rauchhaus, Una
PATENT ASSIGNEE(S):       Novosom A.-G., Germany
SOURCE:                   Ger. Offen., 8 pp.
                          CODEN: GWXXBX
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     DE 10255106        A1   20040609       DE 2002-10255106 20021124
     WO 2004047792      A2   20040610       WO 2003-DE3893   20031124
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
             BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
             MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                  DE 2002-10255106 A  20021124
AB   The invention concerns liposomal formulations that include in the inner
     aqueous phase water-soluble glucocorticoids and the liposomes do not contain
     amphiphilic polymers, e.g. polyethylene glycol-phosphatidyl ethanolamine;
```

liposomes are formed from dipalmitoyl phosphatidyl choline, distearoyl phosphatidyl choline, dipalmitoyl phosphatidyl glycerol, distearoyl phosphatidyl glycerol, distearoyl phosphatidyl serine and cholesterol. Phosphate esters, glucosides and sulfate esters of glucocorticoids are formulated for topical, systemic, oral and rectal administration. The formulations are used as antiinflammatory agents. Thus dexamethasone phosphate was prepared with liposomes composed of palmitoyoleoylphosphatidylcholine, 4-(2-aminoethyl)-morpholino-cholesterol hemisuccinate, cholesteryl hemisuccinate at a ratio of 60:20:20.

IC ICM A61K031-57
ICS A61K009-127

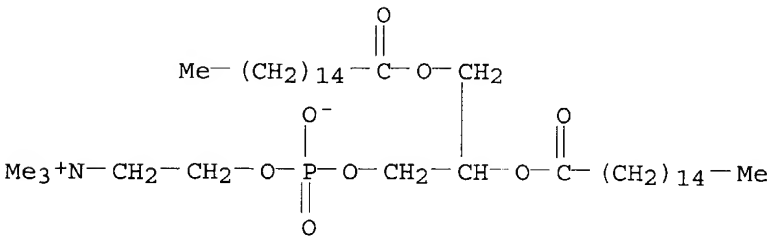
CC 63-6 (Pharmaceuticals)

IT **Drug delivery systems**
(**oral**; liposomal glucocorticoids for use as antiinflammatory agents)

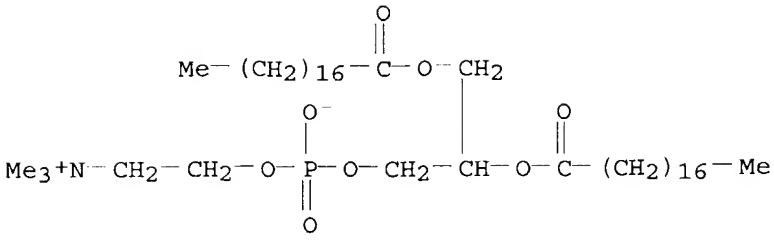
IT 57-88-5, Cholesterol, biological studies 302-25-0, Prednisolone phosphate 312-93-6, Dexamethasone phosphate 360-63-4, Betamethasone phosphate 989-96-8 1510-21-0, Cholesterol hemisuccinate 2203-97-6, Hydrocortisone succinate **2644-64-6**, Dipalmitoyl phosphatidyl choline 2920-86-7, Prednisolone succinate 2921-57-5, Methylprednisolone succinate 3863-59-0, Hydrocortisone phosphate 4537-77-3, Dipalmitoyl phosphatidyl glycerol 4537-78-4, Distearoyl phosphatidyl glycerol **4539-70-2**, Distearoyl phosphatidyl choline 17140-01-1, Prednisolamate hydrochloride 22252-38-6 **26662-91-9**, Palmitoyloleoylphosphatidylcholine 51446-62-9, Distearoyl phosphatidyl serine 57099-40-8 **113669-21-9** 146103-60-8D, Carnosin, acyl derivative 325468-91-5 449791-79-1 452322-62-2 452323-21-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomal glucocorticoids for use as antiinflammatory agents)

IT **2644-64-6**, Dipalmitoyl phosphatidyl choline **4539-70-2**, Distearoyl phosphatidyl choline **26662-91-9**, Palmitoyloleoylphosphatidylcholine **113669-21-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomal glucocorticoids for use as antiinflammatory agents)

RN 2644-64-6 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

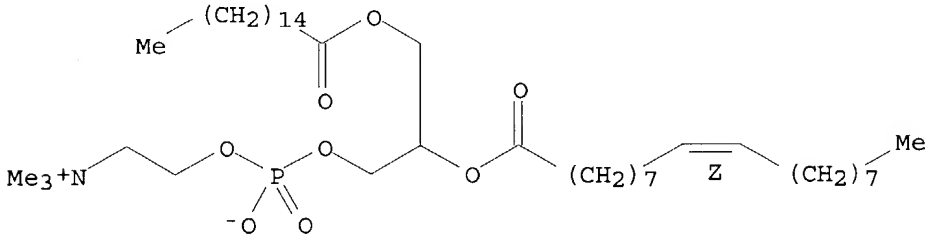


RN 4539-70-2 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 26662-91-9 HCAPLUS
CN 3,5,8-Trioxa-4-phosphahexacos-17-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-9-oxo-7-[[(1-oxohexadecyl)oxy]methyl]-, inner salt, 4-oxide, (17Z)- (9CI) (CA INDEX NAME)

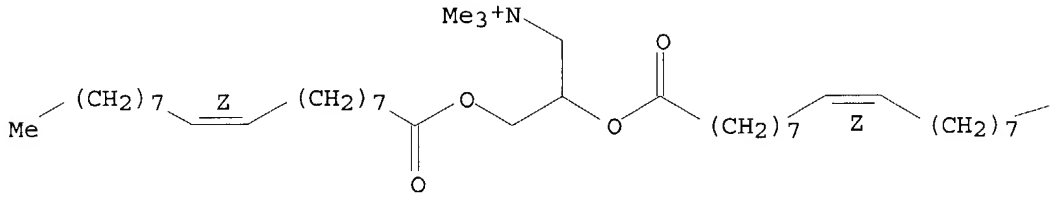
Double bond geometry as shown.



RN 113669-21-9 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

L52 ANSWER 2 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:442650 HCAPLUS
DOCUMENT NUMBER: 141:12281
TITLE: Methods for delivering compounds into a cell
INVENTOR(S): Unger, Evan C.; McCreery, Thomas
PATENT ASSIGNEE(S): Imarx Pharmaceutical Corp., USA
SOURCE: U.S., 41 pp., Cont.-in-part U.S. Ser. No. 785,661, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6743779	B1	20040601	US 1997-841169	19970429
US 5733572	A	19980331	US 1994-346426	19941129
CA 2252617	AA	19971106	CA 1997-2252617	19970430
WO 9740679	A1	19971106	WO 1997-US7237	19970430
W: AU, BR, CA, CN, HU, JP, KR, MX, NO				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9727490	A1	19971119	AU 1997-27490	19970430
AU 736301	B2	20010726		
EP 935415	A1	19990818	EP 1997-921460	19970430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001507207	T2	20010605	JP 1997-539185	19970430
HR 970328	A1	20010430	HR 1997-970328	19970616
US 2001031740	A1	20011018	US 2000-742938	20001221
US 6638767	B2	20031028		

PRIORITY APPLN. INFO.:

US 1994-346426	A2	19941129
US 1996-640554	B2	19960501
US 1997-785661	B2	19970117
US 1989-455707	B2	19891222
US 1990-569828	A2	19900820
US 1991-716899	B2	19910618
US 1991-717084	A2	19910618
US 1993-76239	A2	19930611
US 1993-76250	A2	19930611
US 1993-159674	B2	19931130
US 1993-159687	A2	19931130
US 1993-160232	A2	19931130
US 1994-307305	A2	19940916
US 1997-841169	A	19970429
WO 1997-US7237	W	19970430

AB The present invention is directed, inter alia, to a method for delivering a compound, e.g., a nucleic acid sequence, into a cell comprising administering to the cell the compound to be delivered, an organic halide, and/or a carrier. Ultrasound may also be applied, if desired. For example, in a patient with Duchenne's muscular dystrophy plasmid DNA encoding the gene for dystrophin was injected at multiple sites into the muscles of the thighs and legs, with and without an organic halide. Ultrasound was then applied to the thighs and legs using silicone gel as couplant between the transducer and the patient's skin. The frequency was 200 kHz with a 10% duty cycle and a power level of 1 W. The transducer remained for about 2 to 3 min over any one location on the skin. Enhanced expression for the gene for dystrophin was attained resulting in increased

muscle strength, both with and without the organic halide. Also, the transfection efficiency of cationic lipids with and without an organic halide was evaluated in HeLa cells using lipids DMRIE-C, dioleoylglycero-3 phosphoethylcholine (DODO) and dipalmitoylglycero-3 phosphocholine (DPDO), and perfluorohexane (PFC6). It was shown that perfluorocarbon was effective with a variety of lipids. The enhancement of expression was independent of the type of lipid used. DODO plus PFC6 resulted in about 8 to about 10 fold increase in expression, DMRIE-C resulted in about a 40% enhancement of expression, and DPDO resulted in about a 4-fold increase.

IC ICM A61K031-70
NCL 514044000; 435325000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 3, 8

IT **Drug delivery systems**
(carriers; organic halides, lipid carriers, and optionally ultrasound for intracellular delivery)

IT **Drug delivery systems**
(liposomes; organic halides, lipid carriers, and optionally ultrasound for intracellular delivery)

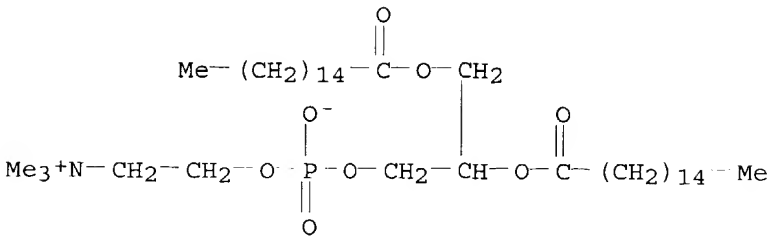
IT **Drug delivery systems**
(microspheres; organic halides, lipid carriers, and optionally ultrasound for intracellular delivery)

IT **DNA**
Dystrophin
Glycolipids
Perfluoro compounds
Perfluorocarbons
Phospholipids, biological studies
Proteins
Sphingolipids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(organic halides, lipid carriers, and optionally ultrasound for intracellular delivery)

IT 76-19-7, Perfluoropropane 307-45-9, Perfluorodecane 355-25-9, Perfluorobutane 355-42-0, n-Perfluorohexane 355-79-3, Perfluorotetrahydropyran 375-48-4, 1-Bromononafluorobutane 423-55-2, 1-Bromoperfluorooctane 678-26-2, Perfluoropentane 2462-63-7 **2644-64-6**, Dipalmitoylphosphatidylcholine 7782-41-4D, Fluorine, compds. 9040-07-7, Chloramphenicol acetyl transferase 19698-29-4, Dipalmitoylphosphatidic acid 71546-79-7 127464-60-2, Vascular endothelial growth factor 145035-97-8, Dipalmitoylphosphatidylethanolamine-PEG **189203-05-2**, DMRIE-C 214127-02-3 216165-62-7 694436-58-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(organic halides, lipid carriers, and optionally ultrasound for intracellular delivery)

IT **2644-64-6**, Dipalmitoylphosphatidylcholine **189203-05-2**, DMRIE-C
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(organic halides, lipid carriers, and optionally ultrasound for intracellular delivery)

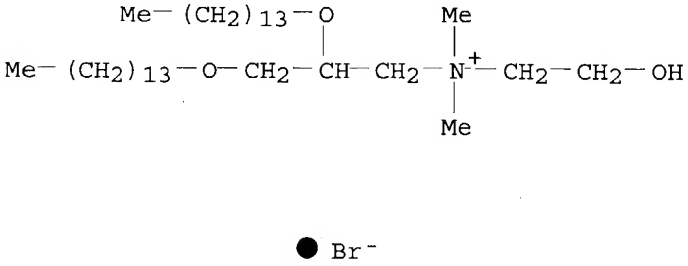
RN 2644-64-6 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 189203-05-2 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, mixt. with N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-1-propanaminium bromide (9CI) (CA INDEX NAME)

CM 1

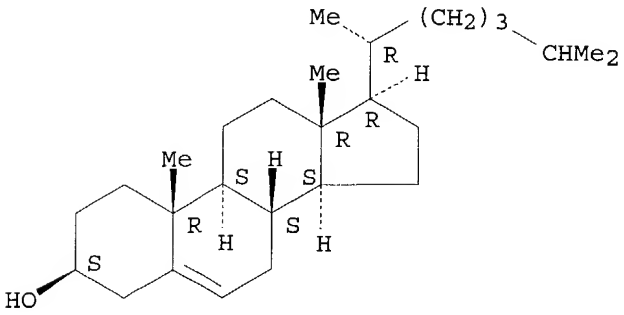
CRN 153312-64-2
CMF C35 H74 N O3 . Br



CM 2

CRN 57-88-5
CMF C27 H46 O

Absolute stereochemistry.



REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 3 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:20328 HCAPLUS
DOCUMENT NUMBER: 140:87674
TITLE: Oligonucleotides for silencing transcription by methylation of cytosines in DNA and their uses, including as antitumor agents
INVENTOR(S): Hu, Ji-Fan; Bowersox, Scott
PATENT ASSIGNEE(S): GMR, USA
SOURCE: U.S. Pat. Appl. Publ., 34 pp., Cont.-in-part of U.S. Ser. No. 643,128.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004006036	A1	20040108	US 2003-422466	20030422

PRIORITY APPLN. INFO.: US 2000-196749P P 20000412
US 2000-214148P P 20000626
US 2000-643128 A2 20000821

AB The invention provides methods and compns. related to oligonucleotides that silence target genes within a cell. The oligonucleotides include an oligonucleotide methylator segment that has a first strand and a second strand complementary to the first strand. The first strand can include at least one m5CG sequence which is paired with an unmethylated CG sequence on the second strand. Alternatively, the first strand can include at least one m5CN1G sequence paired with an unmethylated CN2G sequence on the second strand, wherein N1 is any nucleotide, and N2 is a nucleotide that pairs with N1. The oligonucleotides also include a single-stranded DNA binding segment that is complementary to a nucleotide sequence in the target gene. The DNA binding segment includes at least one m5CG sequence m5CG or at least one 5CN3G sequence, wherein N3 is any nucleotide. The methylator segment and DNA binding segment are operably linked such that the oligonucleotide is capable of inducing methylation at the target nucleotide sequence, thereby silencing the target gene. The putative mechanism is that after binding to the target sequence, the silencing compound forms a semi-methylated hairpin complex in the local chromatin foci. This structure mimics the DNA replication fork structure formed during DNA replication and activates DNA methyltransferase 1 (Dnmt1). Dnmt1 adds a Me group at the 5'-position of cytosine of CpG dinucleotide in the target sequence as it usually does at the replication fork site. DNA methylation spreads, so that the whole DNA region is hypermethylated and the target gene becomes silenced. The examples of the invention show reduced levels of human gene Igf2 mRNA after Hep3B tumor cells were treated with a methylated 22-mer and ability of the same 22-mer to prolong survival in mice that were implanted with Hep3B cells. Oligonucleotides targeted to a CpG island sequence in the Bcl-2 gene inhibited Bcl-2 mRNA and protein production in MCF-7 cells. Oligonucleotide silencing compds. directed against other human genes were also investigated.

IC ICM A61K048-00
ICS C07H021-04
NCL 514044000; 536023100
CC 1-6 (Pharmacology)
Section cross-reference(s): 3, 10, 11, 14, 63
IT **Drug delivery systems**
(liposomes; oligonucleotides for silencing transcription by methylation of cytosines in DNA and their use as antitumor agents)

IT **DNA**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methylation; oligonucleotides for silencing transcription by methylation of cytosines in DNA and their use as antitumor agents)

IT **DNA**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methylcytosine-containing; oligonucleotides for silencing transcription by methylation of cytosines in DNA and their use as antitumor agents)

IT **DNA**
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(thiophosphate-linked; oligonucleotides for silencing transcription by methylation of cytosines in DNA and their use as antitumor agents)

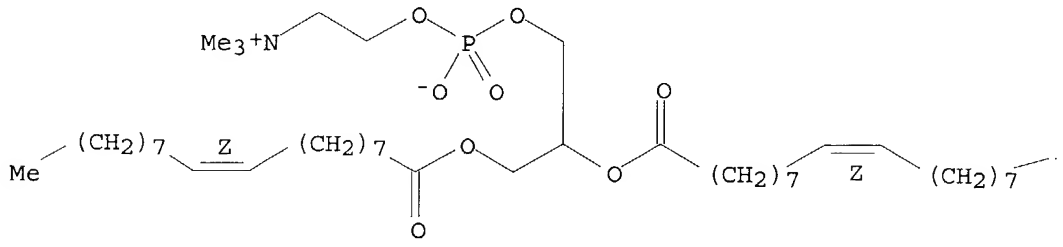
IT 2462-63-7, Dioleoyl phosphatidylethanolamine **68737-67-7**, Dioleoyl phosphatidylcholine **104162-48-3**, N-[1-(2,3-Dioleyloxy)propyl]-n,n,n-trimethylammonium chloride
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(carrier; oligonucleotides for silencing transcription by methylation of cytosines in DNA and their use as antitumor agents)

IT **68737-67-7**, Dioleoyl phosphatidylcholine **104162-48-3**, N-[1-(2,3-Dioleyloxy)propyl]-n,n,n-trimethylammonium chloride
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(carrier; oligonucleotides for silencing transcription by methylation of cytosines in DNA and their use as antitumor agents)

RN 68737-67-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (18Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



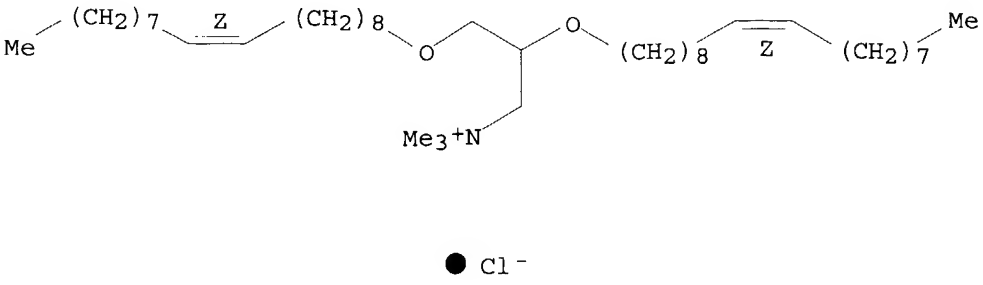
PAGE 1-B

Me

RN 104162-48-3 HCAPLUS

CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L52 ANSWER 4 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:532140 HCAPLUS
DOCUMENT NUMBER: 139:106450
TITLE: Targeted multivalent macromolecules
INVENTOR(S): Wartchow, Charles Aaron; Dechene, Neal Edward; Pease, John S.; Shen, Zhimin; Trulson, Julie; Bednarski, Mark David; Danthi, S. Narasimhan; Zhang, Michael; Choi, Hoyul Steven
PATENT ASSIGNEE(S): Targesome, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 71 pp., Cont.-in-part of U.S. Ser. No. 976,254.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003129223	A1	20030710	US 2002-158777	20020530
US 2002071843	A1	20020613	US 2001-976254	20011011

PRIORITY APPLN. INFO.: US 2000-239684P P 20001011
US 2001-294309P P 20010530
US 2001-309104P P 20010731
US 2001-312435P P 20010815
US 2001-976254 A2 20011011

AB Targeted therapeutic agents, comprising a linking carrier, a therapeutic entity associated with the linking carrier, and at least one targeting entity are provided, as well as methods for their preparation and use. A targeted therapeutic agent is selected from matrix metalloprotease inhibitors, analgesics, aggrecanase inhibitors, alkylating agents, topoisomerase inhibitors, estrogens, androgens, interferons, intercalating agents, kinase modulators, etc. The linking carrier comprises a phosphatidylcholine and is selected from liposomes and a polymerized vesicle. A targeting entity targets a lipid construct to a target selected from a cell surface target, an intracellular target, and an extracellular matrix component. The targeting entity has, e.g., a vascular or tumor cell target selected from chemokine receptors, matrix metalloproteases, integrins, or prostate-specific membrane antigens. For example, integrin-targeted 90Y-labeled peptidomimetic vesicle complexes (IA-NP-Y90)

at 5 μCi/g reduced tumor growth in a melanoma mouse model with average normalized tumor volume less than half the volume in the buffer-treated animals. In addition, the average tumor volume quadrupling time (TVQT) for tumor
treated with IA-NP-Y90 was 15.0 days compared to 6.4 days for tumors treated with buffer.

IC ICM A61K039-395
ICS A61K009-127
NCL 424450000; 424146100; 424178100
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 8, 15

IT **Drug delivery systems**
(liposomes; preparation of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)

IT **Drug delivery systems**
(nanoparticles; preparation of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)

IT **Drug delivery systems**
(particles; preparation of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)

IT Endoglins
Epidermal growth factor receptors
Fibroblast growth factor receptors
Integrins
Platelet-derived growth factor receptors
Pleiotrophins
Prostate-specific antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(targeting of; preparation of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)

IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αv β **5**, targeting of; preparation of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)

IT **75898-25-8DP**, polymer containing 477274-37-6DP, polymer containing 477274-38-7DP, polymer containing **477274-39-8DP**, polymer containing
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(paramagnetic nanoparticles containing; preparation of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)

IT 107-35-7, Taurine 108-30-5, Succinic anhydride, reactions 929-59-9, 1,8-Diamino-3,6-dioxaoctane 6066-82-6, N-Hydroxysuccinimide 25322-68-3, Polyethylene glycol 66990-30-5, 10,12-Tricosadiynoic acid 66990-32-7, 10,12-Pentacosadiynoic acid 77087-60-6 164919-52-2 174665-28-2 477274-38-7 **477274-39-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)

IT **75898-25-8**
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)

IT 57-88-5, Cholesterol, biological studies 120-73-0D, Purine, analogs 289-95-2D, Pyrimidine, analogs **2644-64-6**, DPPC 7689-03-4, Camptothecin 15663-27-1, Cisplatinum **18656-38-7**, DMPC 20830-81-3, Daunorubicin 56420-45-2, Epirubicin 58957-92-9, Idarubicin 88848-80-0 114977-28-5, Docetaxel 123948-87-8, Topotecan
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

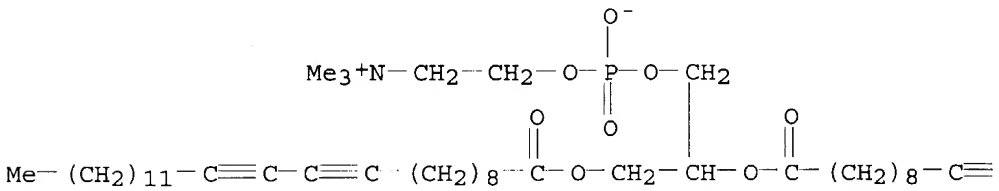
(preparation of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)

IT **75898-25-8DP**, polymer containing **477274-39-8DP**, polymer containing
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(paramagnetic nanoparticles containing; preparation of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)

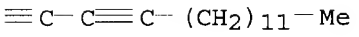
RN 75898-25-8 HCAPLUS

CN 3,5,9-Trioxa-4-phosphatetratriaconta-19,21-diyn-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxo-10,12-pentacosadiynyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

PAGE 1-A



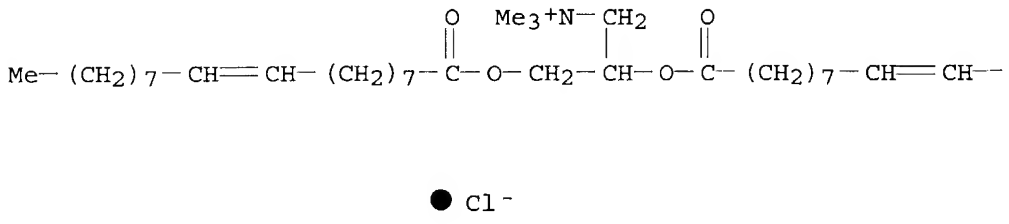
PAGE 1-B



RN 477274-39-8 HCAPLUS

CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(1-oxo-9-octadecenyl)oxy]-, chloride (9CI) (CA INDEX NAME)

PAGE 1-A

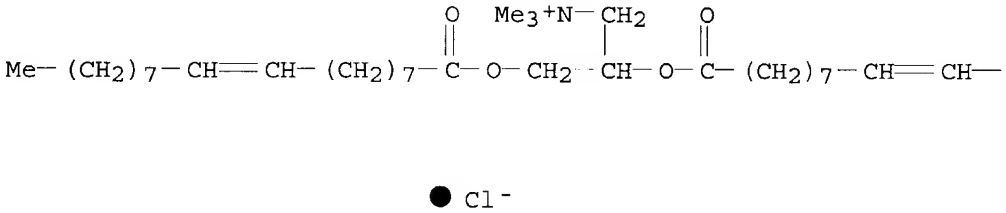


PAGE 1-B

—$(CH_2)_7$—Me

IT **477274-39-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)
RN 477274-39-8 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(1-oxo-9-octadecenyl)oxy]-, chloride (9CI) (CA INDEX NAME)

PAGE 1-A

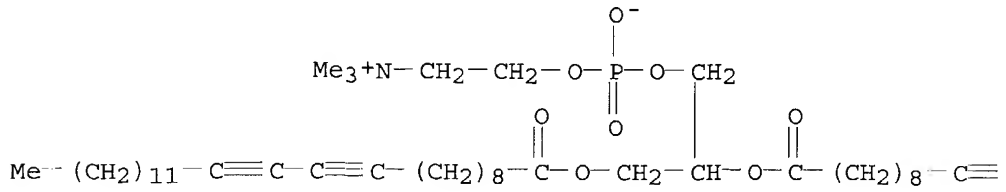


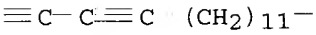
PAGE 1-B

—$(CH_2)_7$—Me

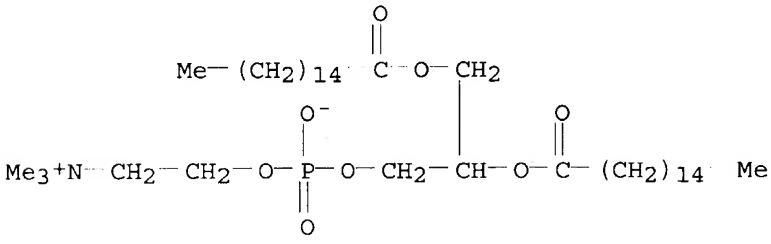
IT **75898-25-8**
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)
RN 75898-25-8 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatetratriaconta-19,21-diyn-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxo-10,12-pentacosadiynyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

PAGE 1-A

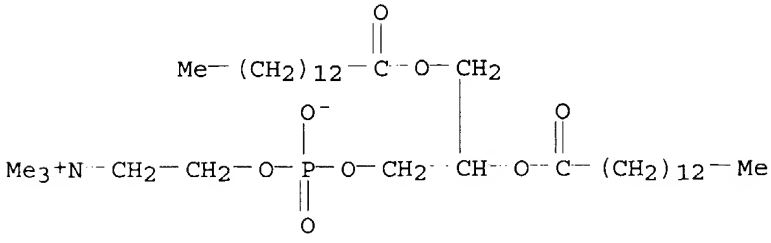




IT **2644-64-6**, DPPC **18656-38-7**, DMPC
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)
RN 2644-64-6 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 18656-38-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatricosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxotetradecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



L52 ANSWER 5 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:395099 HCAPLUS
DOCUMENT NUMBER: 139:64049
TITLE: Three-dimensional imaging of lipid gene-carriers: Membrane charge density controls universal transfection behavior in lamellar cationic liposome-DNA complexes

AUTHOR(S): Lin, Alison J.; Slack, Nelle L.; Ahmad, Ayesha; George, Cyril X.; Samuel, Charles E.; Safinya, Cyrus R.
CORPORATE SOURCE: Materials Department, Physics Department, University of California, Santa Barbara, CA, 93106, USA
SOURCE: Biophysical Journal (2003), 84(5), 3307-3316
CODEN: BIOJAU; ISSN: 0006-3495
PUBLISHER: Biophysical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cationic liposomes (CLs) are used worldwide as gene vectors (carriers) in nonviral clin. applications of gene delivery, albeit with unacceptably low transfection efficiencies (TE). The authors present three-dimensional laser scanning confocal microscopy studies revealing distinct interactions between CL-DNA complexes, for both lamellar LCα and inverted hexagonal HCII nanostructures, and mouse fibroblast cells. Confocal images of LCα complexes in cells identified two regimes. For low membrane charge d. (σM), DNA remained trapped in CL-vectors. By contrast, for high σM, released DNA was observed in the cytoplasm, indicative of escape from endosomes through fusion. Remarkably, firefly luciferase reporter gene studies in the highly complex LCα-mammalian cell system revealed an unexpected simplicity where, at a constant cationic to anionic charge ratio, TE data for univalent and multivalent cationic lipids merged into a single curve as a function of σM, identifying it as a key universal parameter. The universal curve for transfection by LCα complexes climbs exponentially over ≈ four decades with increasing σM below an optimal charge d. (σ*M), and sats. for σM > σ*M at a value rivaling the high transfection efficiency of HCII complexes. In contrast, the transfection efficiency of HCII complexes is independent of σM. The exponential dependence of TE on σM for LCα complexes, suggests the existence of a kinetic barrier against endosomal fusion, where an increase in σM lowers the barrier. In the saturated TE regime, for both LCα complexes and HCII, confocal microscopy reveals the dissociation of lipid and DNA. However, the lipid-released DNA is observed to be in a condensed state, most likely with oppositely charged macro-ion condensing agents from the cytoplasm, which remain to be identified. Much of the observed bulk of condensed DNA may be transcriptionally inactive and may determine the current limiting factor to transfection by cationic lipid gene vectors.

CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1

IT **DNA**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(complexes; three-dimensional laser scanning confocal microscopy shows membrane charge d. controls transfection behavior in lamellar cationic liposome-DNA complexes)

IT **Drug delivery systems**
(liposomes, cationic; three-dimensional laser scanning confocal microscopy shows membrane charge d. controls transfection behavior in lamellar cationic liposome-DNA complexes)

IT **153312-64-2**, DMRIE **282533-23-7**, DOSPA
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(cationic liposomes containing DOPC and DOTAP; three-dimensional laser scanning confocal microscopy shows membrane charge d. controls transfection behavior in lamellar cationic liposome-DNA complexes)

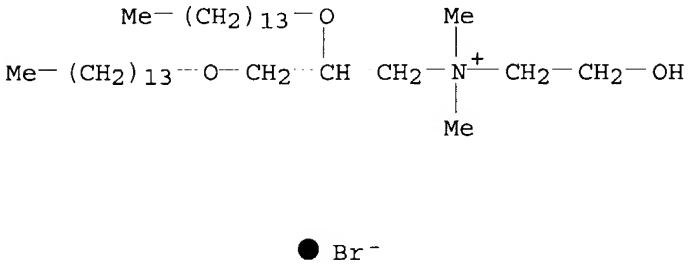
IT **144189-73-1**, DOTAP
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL

(Biological study)
(cationic liposomes containing DOPC or DOPE and DOTAP; three-dimensional laser scanning confocal microscopy shows membrane charge d. controls transfection behavior in lamellar cationic liposome-DNA complexes)

IT **4235-95-4**, DOPC
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(cationic liposomes containing DOTAP, DMRIE, or DOSPA and; three-dimensional laser scanning confocal microscopy shows membrane charge d. controls transfection behavior in lamellar cationic liposome-DNA complexes)

IT **153312-64-2**, DMRIE **282533-23-7**, DOSPA
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(cationic liposomes containing DOPC and DOTAP; three-dimensional laser scanning confocal microscopy shows membrane charge d. controls transfection behavior in lamellar cationic liposome-DNA complexes)

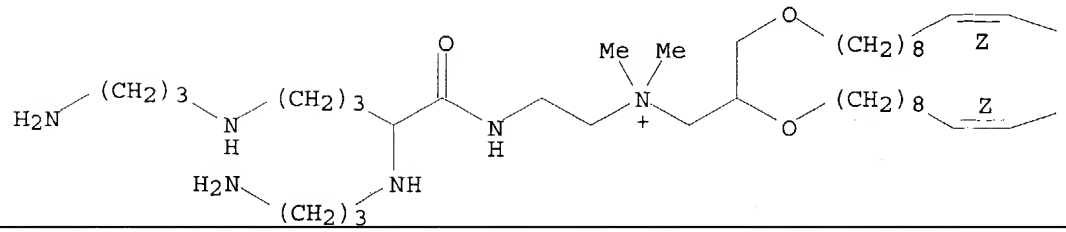
RN 153312-64-2 HCAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



RN 282533-23-7 HCAPLUS
CN 1-Propanaminium, N-[2-[[2,5-bis[(3-aminopropyl)amino]-1-oxopentyl]amino]ethyl]-N,N-dimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride, tetrahydrochloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

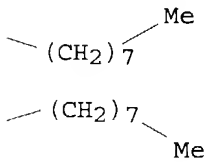
PAGE 1-A



● Cl^-

● 4 HCl

PAGE 1-B



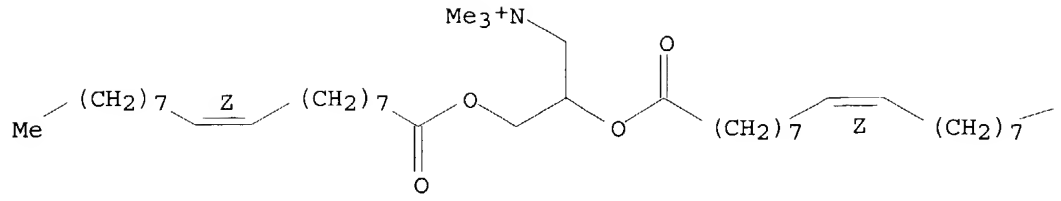
IT **144189-73-1**, DOTAP
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(cationic liposomes containing DOPC or DOPE and DOTAP; three-dimensional laser scanning confocal microscopy shows membrane charge d. controls transfection behavior in lamellar cationic liposome-DNA complexes)
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

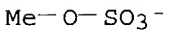
PAGE 1-A



PAGE 1-B

CM 2

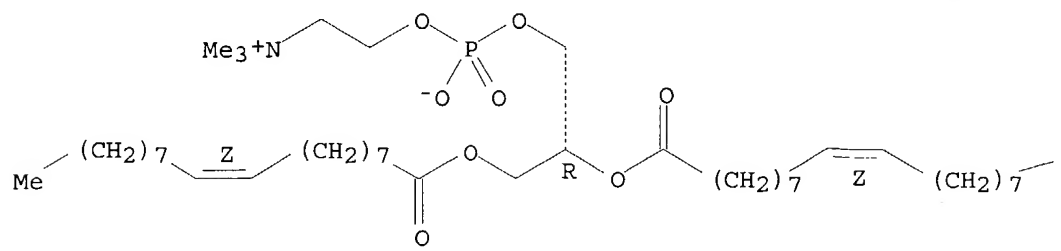
CRN 21228-90-0
CMF C H3 O4 S



IT **4235-95-4**, DOPC
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(cationic liposomes containing DOTAP, DMRIE, or DOSPA and; three-dimensional laser scanning confocal microscopy shows membrane charge d. controls transfection behavior in lamellar cationic liposome-DNA complexes)
RN 4235-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



Me

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 6 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:376681 HCAPLUS
DOCUMENT NUMBER: 138:384141
TITLE: Liposome-encapsulated immunostimulatory sequences as mucosal adjuvants
INVENTOR(S): Semple, Sean; Klimuk, Sandra; Yuan, Zuan-Ning
PATENT ASSIGNEE(S): Inex Pharmaceuticals Corporation, Can.
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003039595	A2	20030515	WO 2002-CA1717	20021107
WO 2003039595	A3	20030918		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004009943	A1	20040115	US 2003-437263	20030512
US 2004013649	A1	20040122	US 2003-437258	20030512

PRIORITY APPLN. INFO.:

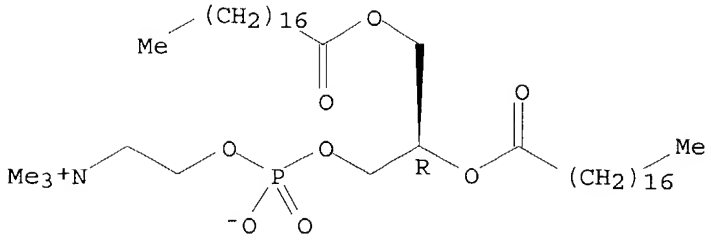
US 2001-337522P	P	20011107
US 2002-379343P	P	20020510
US 1999-151211P	P	19990827
US 2000-176406P	P	20000113
US 2000-649527	A	20000828
US 2003-454298P	P	20030312
US 2003-460646P	P	20030404

AB The authors disclose an enhancement of mucosal immune responses to antigens using to lipid-nucleic acids (LNA) formulations. In one example, the local (lung) and distant (vaginal) mucosal IgA response to nasal **immunization** with target antigen was enhanced by liposome-encapsulated immunostimulatory sequences.

IC ICM A61K039-39

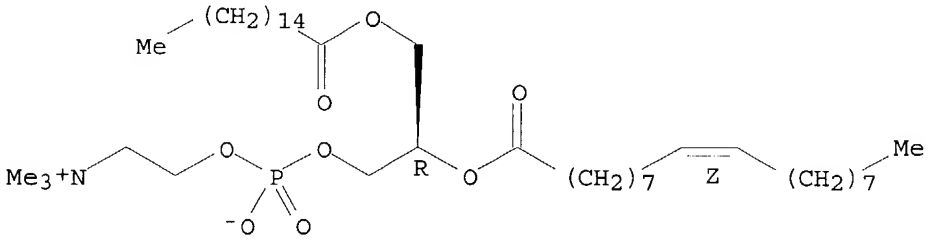
ICS A61P037-04
CC 15-2 (Immunochemistry)
Section cross-reference(s): 63
ST liposome CpG oligodeoxynucleotide mucosal **vaccine**
IT Phosphorothioate oligodeoxyribonucleotides
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CpG-containing; liposome-encapsulated immunostimulatory sequences as mucosal adjuvants for mucosal **immunization**)
IT Immunostimulants
(adjuvants; liposome-encapsulated immunostimulatory sequences as mucosal adjuvants for mucosal **immunization**)
IT **Antigens**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates; to liposomes of encapsulated immunostimulatory sequences)
IT **Antigens**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipidated; for capture by liposomes of encapsulated immunostimulatory sequences)
IT **Drug delivery systems**
(liposomes; for immunostimulatory sequences as mucosal adjuvants)
IT **Immunity**
(mucosal; liposome-encapsulated immunostimulatory sequences as mucosal adjuvants for enhancement of)
IT **Vaccines**
(nasal; liposome-encapsulated immunostimulatory sequences as mucosal adjuvants for)
IT **DNA**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thiophosphate-linked, CpG-containing; liposome-encapsulated immunostimulatory sequences as mucosal adjuvants for mucosal **immunization**)
IT 57-88-5, Cholesterol, biological studies **816-94-4**, DSPC 3700-67-2, DDAB 4004-05-1, DOPE 7212-69-3, DODAC **26853-31-6**, POPC 104162-59-6, DODMA 124050-77-7, DOGS 127512-29-2, DODAP **132172-61-3**, DOTAP chloride 137056-72-5, DC-chol **153312-64-2**, DMRIE 160743-62-4 **168479-03-6**, DOSPA
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of liposomes encapsulating immunostimulatory sequences)
IT **816-94-4**, DSPC **26853-31-6**, POPC **132172-61-3**, DOTAP chloride **153312-64-2**, DMRIE **168479-03-6**, DOSPA
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of liposomes encapsulating immunostimulatory sequences)
RN 816-94-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 26853-31-6 HCAPLUS
CN 3,5,8-Trioxa-4-phosphahexacos-17-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-9-oxo-7-[[(1-oxohexadecyl)oxy]methyl]-, inner salt, 4-oxide, (7R,17Z)- (9CI) (CA INDEX NAME)

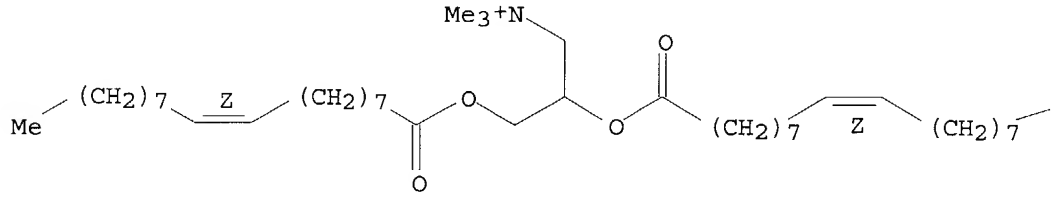
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 132172-61-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

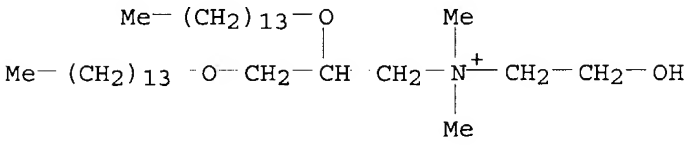
PAGE 1-A



● Cl⁻

PAGE 1-B

RN 153312-64-2 HCAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



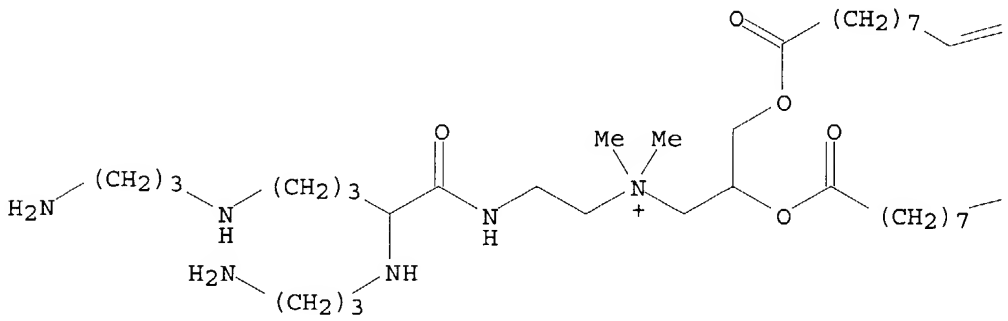
RN 168479-03-6 HCAPLUS
CN 1-Propanaminium, N-[2-[[2,5-bis[(3-aminopropyl)amino]-1-oxopentyl]amino]ethyl]-N,N-dimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, salt with trifluoroacetic acid (1:1) (9CI) (CA INDEX NAME)

CM 1

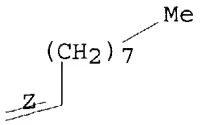
CRN 168479-02-5
CMF C54 H107 N6 O5

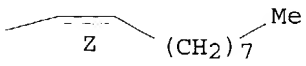
Double bond geometry as shown.

PAGE 1-A



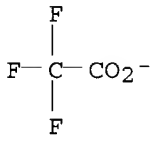
PAGE 1-B





CM 2

CRN 14477-72-6
CMF C2 F3 O2



L52 ANSWER 7 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:5751 HCAPLUS
DOCUMENT NUMBER: 138:78447
TITLE: A method for preparation of vesicles loaded with biological material and different uses thereof
INVENTOR(S): Barenholz, Yechezkel; Kedar, Eliezer
PATENT ASSIGNEE(S): Yissum Research Development Company of the Hebrew University of Jerusalem, Israel
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000227	A2	20030103	WO 2002-IL506	20020625
WO 2003000227	A3	20031113		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1404298 A2 20040407 EP 2002-738605 20020625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: US 2001-300065P P 20010625
WO 2002-IL506 W 20020625

AB The present invention discloses a method for an efficient entrapment of active biol. material in liposomes. The method is based on the steps of drying a suspension of liposome-forming lipids and then hydrating the dry composition obtained with an aqueous solution containing a biol. active material to be entrapped in high yield in the liposomes thus formed. The invention also concerns liposomal formulations produced by the method of the invention and their uses.

IC ICM A61K009-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 15

IT **RNA**
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(interfering; method for preparation of liposomal vesicles loaded with biol. material and different uses thereof)

IT **Drug delivery systems**
(liposomes; method for preparation of liposomal vesicles loaded with biol. material and different uses thereof)

IT Cell membrane
Freeze drying
Mitochondria
Physiological saline solutions
Polar solvents
Ribosome
Vaccines
Viral vectors
(method for preparation of liposomal vesicles loaded with biol. material and different uses thereof)

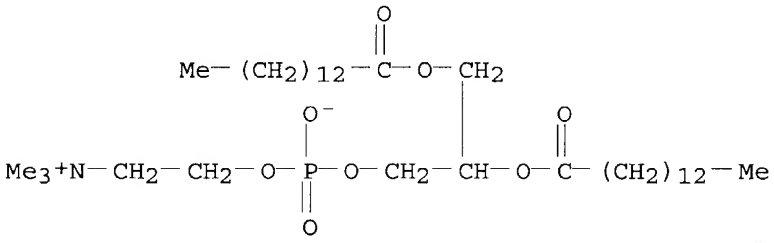
IT Antibodies and Immunoglobulins
Antigens
Antisense DNA
Antisense RNA
Cytokines
DNA
Enzymes, biological studies
Growth factors, animal
Nucleotides, biological studies
Phosphatidylinositols
Phosphatidylserines
Phospholipids, biological studies
Sphingolipids
Sphingomyelins
Sphingomyelins
Zymogens
mRNA
rRNA
tRNA
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);

USES (Uses)
(method for preparation of liposomal vesicles loaded with biol. material and different uses thereof)

IT 6254-89-3, N-Palmitoylsphingomyelin **18656-38-7**, Dimyristoyl phosphatidylcholine 25322-68-3D, Polyethyleneglycol, lipid conjugates 58909-84-5, N-Stearoylsphingomyelin 60037-60-7 61361-72-6, Dimyristoyl phosphatidylglycerol 94359-13-4 108392-10-5 **144189-73-1**, Dotap **168479-02-5 173666-09-6**, DSTAP **197974-74-6**
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
USES (Uses)
(method for preparation of liposomal vesicles loaded with biol. material and different uses thereof)

IT **18656-38-7**, Dimyristoyl phosphatidylcholine **144189-73-1**, Dotap **168479-02-5 173666-09-6**, DSTAP **197974-74-6**
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
USES (Uses)
(method for preparation of liposomal vesicles loaded with biol. material and different uses thereof)

RN 18656-38-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatricosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxotetradecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



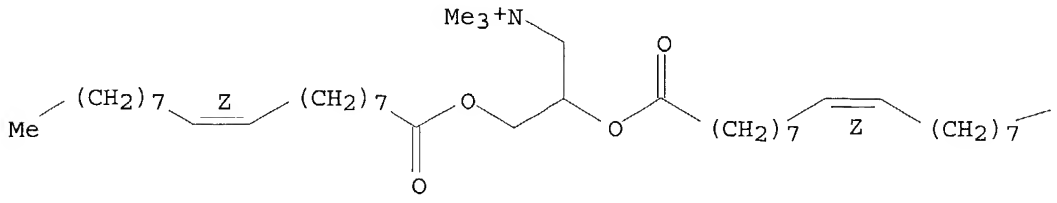
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

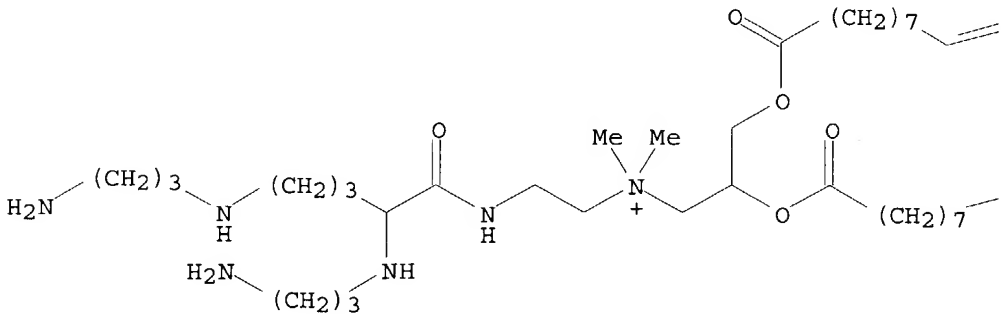
CRN 21228-90-0
CMF C H3 O4 S

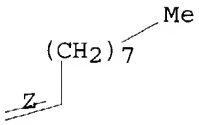
Me O SO_3^-

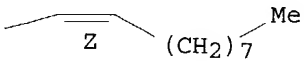
RN 168479-02-5 HCAPLUS
CN 1-Propanaminium, N-[2-[[2,5-bis[(3-aminopropyl)amino]-1-oxopentyl]amino]ethyl]-N,N-dimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

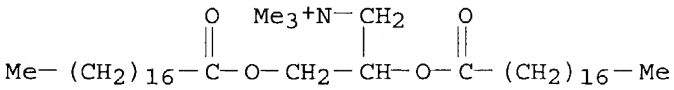
PAGE 1-A



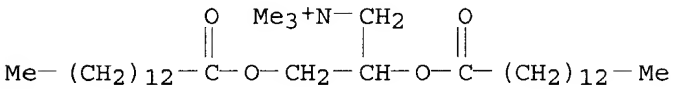




RN 173666-09-6 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)



RN 197974-74-6 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(1-oxotetradecyl)oxy]-, chloride (9CI) (CA INDEX NAME)



L52 ANSWER 8 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:945750 HCAPLUS
DOCUMENT NUMBER: 139:202221
TITLE: A Lipid-based Delivery System for Antisense Oligonucleotides Derived from a Hydrophobic Complex
AUTHOR(S): Wong, F. M. P.; MacAdam, S. A.; Kim, A.; Oja, C.; Ramsay, E. C.; Bally, M. B.
CORPORATE SOURCE: Cancer Agency, Department of Advanced Therapeutics, Vancouver, BC, V5Z 1L3, Can.
SOURCE: Journal of Drug Targeting (2002), 10(8), 615-623
CODEN: JDTAEH; ISSN: 1061-186X
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Antisense oligodeoxynucleotides (ASOs) prevent expression of proteins by

binding to specific regions of mRNA. This report investigates a potential lipid-based delivery system for ASO. A hydrophobic complex was recovered following addition of cationic lipids to ASOs in a Bligh and Dyer monophase [chloroform/methanol/water (1:2.1:1, volume/volume/v)]. The addition of monovalent cationic lipids (dioleyldimethylammonium chloride, dimethyldioctadecylammonium bromide, dioleoyltrimethylammonium propane), resulted in >95 recovery of the ASOs from the organic phase when ASO phosphate charge was neutralized. Cholesteryldimethylaminoethylcarbamate mediated efficient extraction at a charge ratio (+/-) >5.2. ASOs could not be extracted into the organic phase by the polyvalent lipids, dioctadecylamidoglycyl spermine and 2,3-dioleyloxy-N-[2(sperminecarboxamido)ethyl]-N,N-dimethyl-1-propaminium trifluoroacetate, even at a charge ratio (+/-) >5. Dioleoylphosphatidylethanolamine, but not dioleoylphosphatidylcholine, prevented formation and destabilized the hydrophobic complexes. The characterization of the hydrophobic complex led to the development of lipid-ASO particles containing dioleyldimethylammonium chloride, dioleoylphosphatidylethanolamine and poly(ethylene glycol)-conjugated phosphatidylethanolamine (LAPs). When FITC-labeled ASOs in LAPs were added to B-cell lymphoma cells (DoHH2) in vitro, cell-associated ASO decreased as poly(ethylene glycol)-conjugated phosphatidylethanolamine incorporation increased. Western Blot anal. demonstrated that no significant downregulation of Bcl-2 protein was observed when using LAPs. The results suggest that the use of stabilized PEG-conjugated lipids may be detrimental for cationic lipid-based ASO delivery.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 3

IT **Drug delivery systems**
(lipid-based delivery system for antisense oligonucleotides)

IT **Antisense oligonucleotides**
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid-based delivery system for antisense oligonucleotides)

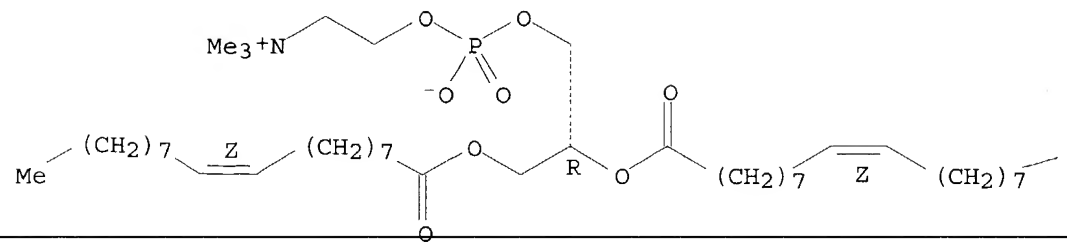
IT 2462-63-7, Dope 3700-67-2, Dimethyldioctadecylammonium bromide **4235-95-4**, Dopc 7212-69-3, N,N-Dioleyl-N,N-dimethylammonium chloride 124050-77-7, Transfectam 137056-72-5, DC-Chol **144189-73-1**, Dotap 145035-96-7, Dspe-PEG **158571-62-1**, Lipofectamine 211567-66-7, Dmpe-PEG
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid-based delivery system for antisense oligonucleotides)

IT **4235-95-4**, Dopc **144189-73-1**, Dotap **158571-62-1**, Lipofectamine
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid-based delivery system for antisense oligonucleotides)

RN 4235-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

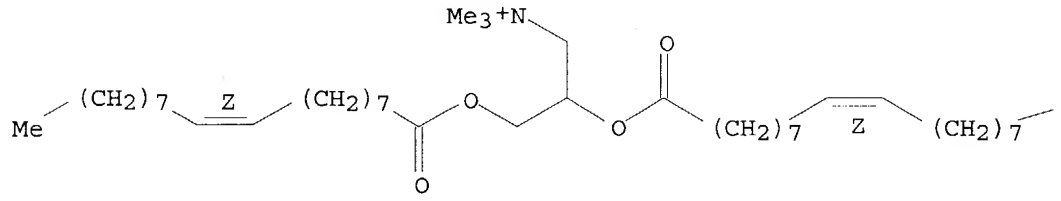
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A

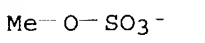


PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S



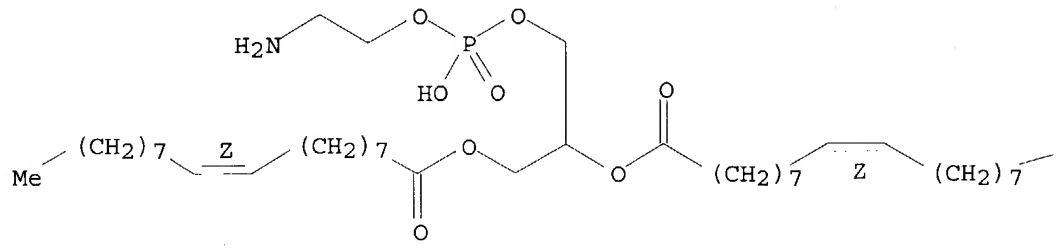
RN 158571-62-1 HCAPLUS
CN 1-Propanaminium, N-[3-[[3-[[4-[(3-aminopropyl)amino]butyl]amino]propyl]amino]-3-oxopropyl]-N,N-dimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, salt with trifluoroacetic acid (1:1), mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

CM 2

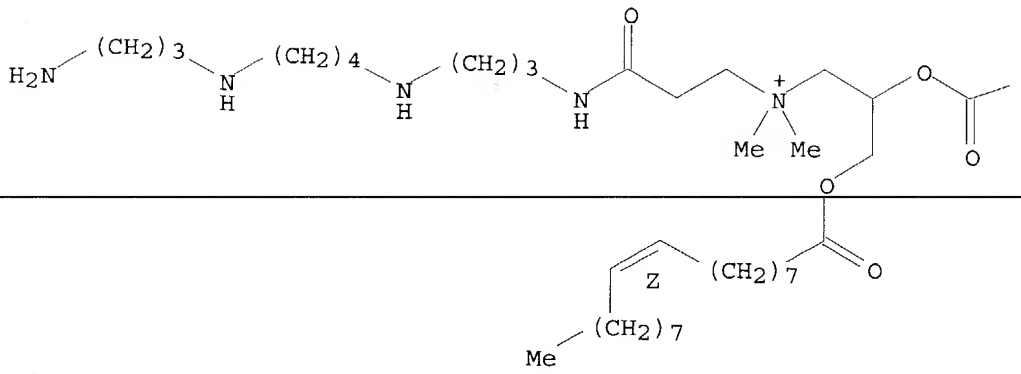
CRN 185097-43-2
CMF C54 H106 N5 O5 . C2 F3 O2

CM 3

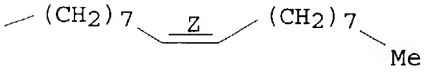
CRN 181508-68-9
CMF C54 H106 N5 O5

Double bond geometry as shown.

PAGE 1-A

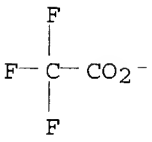


PAGE 1-B



CM 4

CRN 14477-72-6
CMF C2 F3 O2

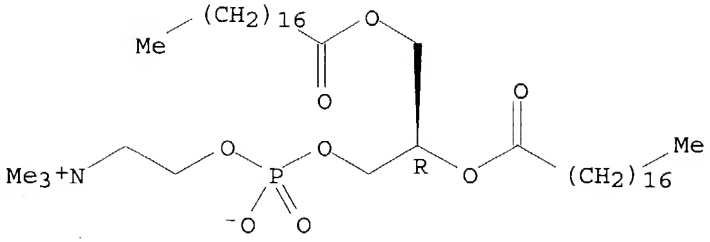


REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 9 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:929722 HCAPLUS
DOCUMENT NUMBER: 139:169107
TITLE: Immersion delivery of plasmid DNA I. A study of the potentials of a liposomal delivery system in rainbow trout (Oncorhynchus mykiss) fry
AUTHOR(S): Romoren, Kristine; Thu, Beate J.; Smistad, Gro; Evensen, Oystein
CORPORATE SOURCE: School of Pharmacy, Department of Pharmaceutics, University of Oslo, Oslo, N-0316, Norway
SOURCE: Journal of Controlled Release (2002), 85(1-3), 203-213
CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A successful regime for i.m. injection of naked DNA is developed in fish, but the exploration of other ways of administration has not yet been studied in any detail. Immersion is a delivery route offering many advantages compared to conventional ways of administration. Applying cationic liposomes as a delivery system for DNA by this route, however, is met with severe toxicity problems. In this report, the underlying mechanisms of the acute toxicity were investigated in vivo and in vitro. The most critical factor was found to be the charge of the liposomes. Cationic liposomes above a certain threshold concentration had a lethal effect in rainbow trout fry. In contrast, similar concns. of neutral or anionic liposomes were not toxic. Furthermore, large liposome-mucin complexes were formed upon addition of mucin to cationic liposomes. This was not observed with neutral or anionic liposomes. Lipoplexes were less toxic and interacted less with mucin compared to cationic liposomes. Hence, the mechanism of the acute toxicity in rainbow trout fry is suggested to be an interaction between the cationic liposomes and anionic components of gill mucin. The consequence is hypoxia and this is most likely the cause of acute toxicity observed in rainbow trout fry.
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 3
ST rainbow trout plasmid DNA **vaccine** delivery liposome
IT **DNA**
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(complexes; immersion delivery of DNA via liposomes in rainbow trout)
IT Adhesion, biological
Oncorhynchus mykiss
Particle size
Plasmid vectors
Vaccines
Zeta potential
(immersion delivery of DNA via liposomes in rainbow trout)
IT **Drug delivery systems**
(liposomes; immersion delivery of DNA via liposomes in rainbow trout)
IT **816-94-4**, DSPC 4004-05-1, DOPE **144189-73-1**, DOTAP
217939-97-4, DSPG
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(immersion delivery of DNA via liposomes in rainbow trout)
IT **816-94-4**, DSPC **144189-73-1**, DOTAP
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(immersion delivery of DNA via liposomes in rainbow trout)
RN 816-94-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



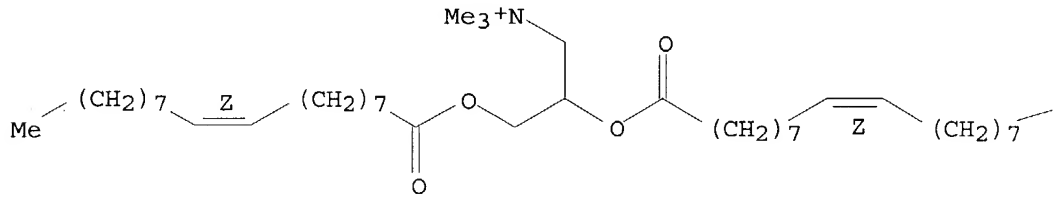
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

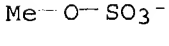
PAGE 1-A



PAGE 1-B

CM 2

CRN 21228-90-0
CMF C H3 O4 S

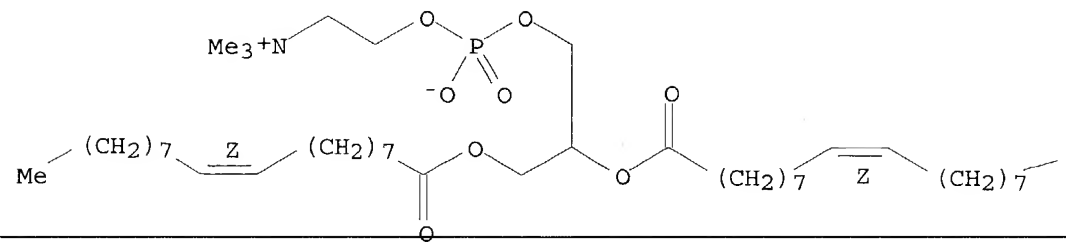


REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 10 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:857754 HCAPLUS
DOCUMENT NUMBER: 139:73849
TITLE: A new approach for the study of cationic lipid-DNA complexes by energy dispersive X-ray diffraction
AUTHOR(S): Caracciolo, G.; Caminiti, R.; Natali, F.; Congiu Castellano, A.
CORPORATE SOURCE: Dipartimento di Fisica and INFM, Universita 'La Sapienza', Rome, IT-00185, Italy
SOURCE: Chemical Physics Letters (2002), 366(3,4), 200-204
CODEN: CHPLBC; ISSN: 0009-2614
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB X-ray diffraction (XRD) studies on the cationic liposome (CL)-DNA complexes currently used in gene delivery have provided detailed structural informations on these compact, ordered self-assemblies sheding light on the poorly understood structure-activity relationship. Among these, the expts. carried out by using a synchrotron radiation source have showed an exptl. resolution remarkably better than that achieved one by traditional in house apparatuses. Here we show a new exptl. approach for the study of CL-DNA complexes, based on the employment of silicon wafers as substrates, which allows obtaining high-resolution structural informations by energy dispersive X-ray diffraction (EDXD).
CC 63-5 (Pharmaceuticals)
IT **DNA**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(complexes; study of cationic lipid-DNA complexes by energy dispersive X-ray diffraction)
IT **Drug delivery systems**
(liposomes; study of cationic lipid-DNA complexes by energy dispersive X-ray diffraction)
IT **68737-67-7**, Dioleoyl phosphatidylcholine **144189-73-1**, Dotap
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(study of cationic lipid-DNA complexes by energy dispersive X-ray diffraction)
IT **68737-67-7**, Dioleoyl phosphatidylcholine **144189-73-1**, Dotap
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(study of cationic lipid-DNA complexes by energy dispersive X-ray diffraction)
RN 68737-67-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (18Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

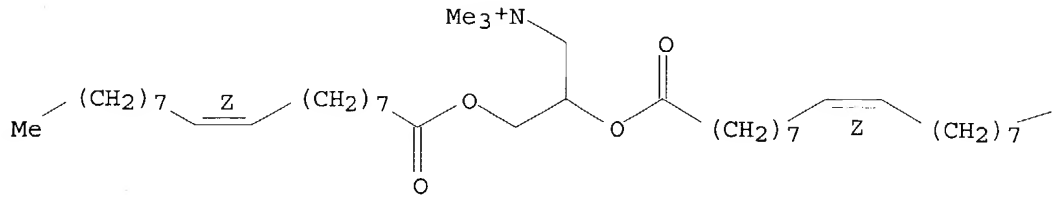
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A

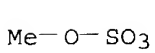


PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 11 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:849401 HCAPLUS
DOCUMENT NUMBER: 137:342088
TITLE: Lipid-based formulations for gene transfer
INVENTOR(S): MacLachlan, Ian
PATENT ASSIGNEE(S): Protiva Biotherapeutics Inc., Can.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002087541	A1	20021107	WO 2002-CA669	20020430
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003077829	A1	20030424	US 2002-136707	20020430

PRIORITY APPLN. INFO.: US 2001-287796P P 20010430

AB The present invention provides lipid-based formulations for delivering nucleic acids to a cell, and assays for optimizing the transfection efficiency of such lipid-based formulations.

IC ICM A61K009-127
ICS A61K048-00; A61K047-48
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 3
IT **Drug delivery systems**
(carriers; lipid-based formulations for gene transfer)
IT **Nucleic acids**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid-based formulations for gene transfer)
IT **Antisense oligonucleotides**
DNA
Ribozymes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);

USES (Uses)
(lipid-based formulations for gene transfer)

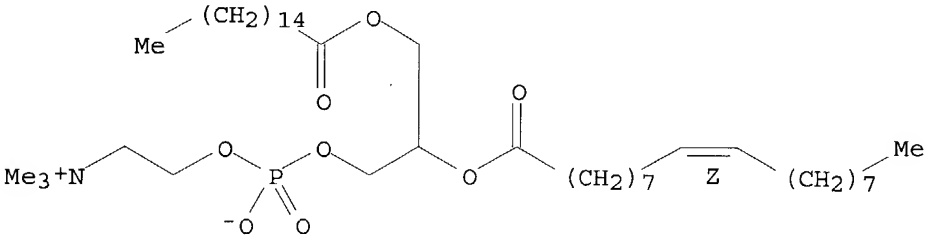
IT **Drug delivery systems**
(liposomes; lipid-based formulations for gene transfer)

IT 2462-63-7, Dope 7212-69-3, Dodac **26662-91-9**, POPC
104162-47-2 **104162-48-3**, Dotma **144189-73-1**, Dotap
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid-based formulations for gene transfer)

IT **26662-91-9**, POPC **104162-48-3**, Dotma **144189-73-1**
, Dotap
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid-based formulations for gene transfer)

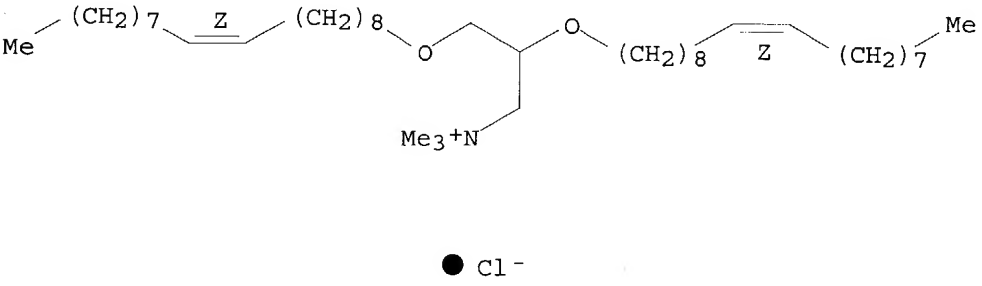
RN 26662-91-9 HCAPLUS
CN 3,5,8-Trioxa-4-phosphahexacos-17-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-9-oxo-7-[[(1-oxohexadecyl)oxy]methyl]-, inner salt, 4-oxide, (17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 104162-48-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



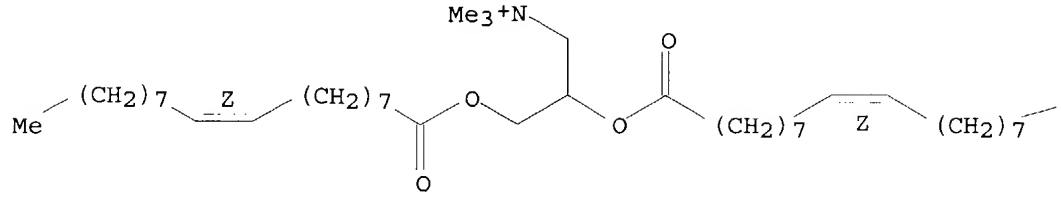
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me— O— SO_3^-

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 12 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:789682 HCAPLUS
DOCUMENT NUMBER: 137:273730
TITLE: Efficient synthesis and cell-transfection properties of a new multivalent cationic lipid for nonviral gene delivery
AUTHOR(S): Ewert, Kai; Ahmad, Ayesha; Evans, Heather M.; Schmidt, Hans-Werner; Safinya, Cyrus R.
CORPORATE SOURCE: Department of Materials, University of California, Santa Barbara, CA, 93106, USA
SOURCE: Journal of Medicinal Chemistry (2002), 45(23), 5023-5029
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lipid-mediated delivery of DNA into cells holds great promise both for

gene therapy and basic research applications. This paper describes the efficient and facile synthesis and the characterization of a new multivalent cationic lipid with a double-branched headgroup structure for gene delivery applications. The synthetic scheme can be extended to give cationic lipids of different charge, spacer, or lipid chain length. The chemical and phys. properties of self-assembled complexes of the cationic liposomes (CLs) with DNA give indications of why multivalent cationic lipids possess superior transfection properties. The lipid bears a headgroup with five charges in the fully protonated state, which is attached to an unsatd. double-chain hydrophobic moiety based on 3,4-dihydroxybenzoic acid. Liposomes consisting of the new multivalent lipid and the neutral lipid 1,2-dioleoyl-sn-glycerophosphatidylcholine (DOPC) were used to prepare complexes with DNA. Investigations of the structures of these complexes by optical microscopy and small-angle X-ray scattering reveal a lamellar LαC phase of CL-DNA complexes with the DNA mols. sandwiched between bilayers of the lipids. Expts. using plasmid DNA containing the firefly luciferase reporter gene show that these complexes efficiently transfect mammalian cells. When compared to the monovalent cationic lipid 2,3-dioleyloxypropyltrimethylammonium chloride (DOTAP), the higher charge d. of the membranes of CL-DNA complexes achievable with the new multivalent lipid greatly increases transfection efficiency in the regime of small molar ratios of cationic to neutral lipid. This is desired to minimize the known toxicity effects of cationic lipids.

CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 21

IT **DNA**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(complexes, CL-DNA complexes; efficient synthesis and cell-transfection properties of a new multivalent cationic lipid for nonviral gene delivery)

IT **Drug delivery systems**
(liposomes, cationic, with DNA; efficient synthesis and cell-transfection properties of a new multivalent cationic lipid for nonviral gene delivery)

IT **4235-95-4**, DOPC
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(efficient synthesis and cell-transfection properties of a new multivalent cationic lipid for nonviral gene delivery)

IT 99-50-3, 3,4-Dihydroxybenzoic acid **144189-73-1**, DOTAP
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(efficient synthesis and cell-transfection properties of a new multivalent cationic lipid for nonviral gene delivery)

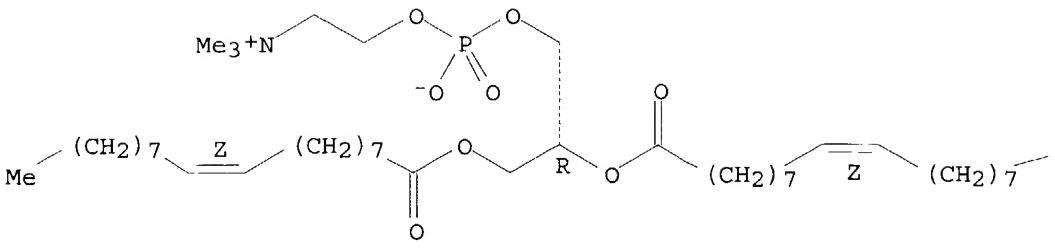
IT **4235-95-4**, DOPC
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(efficient synthesis and cell-transfection properties of a new multivalent cationic lipid for nonviral gene delivery)

RN 4235-95-4 HCAPLUS

CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

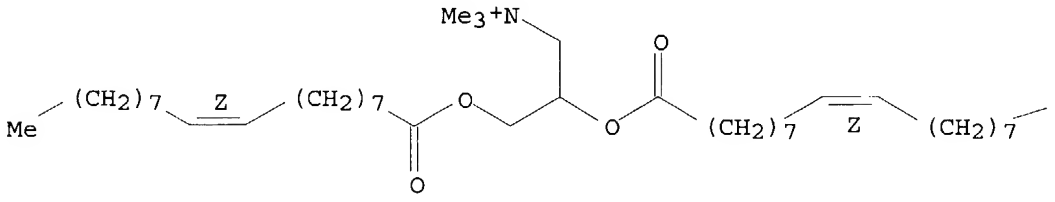
IT **144189-73-1**, DOTAP
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(efficient synthesis and cell-transfection properties of a new multivalent cationic lipid for nonviral gene delivery)
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO_3^-

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 13 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:681698 HCAPLUS
DOCUMENT NUMBER: 138:343566
TITLE: Liposome (Lipodine)-mediated DNA **vaccination** by the oral route
AUTHOR(S): Perrie, Yvonne; Obrenovic, Mia; McCarthy, David; Gregoriadis, Gregory
CORPORATE SOURCE: Pharmaceutical Sciences Research Institute, Aston University, Birmingham, UK
SOURCE: Journal of Liposome Research (2002), 12(1 & 2), 185-197
CODEN: JLREE7; ISSN: 0898-2104
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Plasmid DNA pRc/CMV HBS encoding the S (small) region of hepatitis B surface antigen (HBsAg) was incorporated by the dehydration-rehydration method into Lipodine liposomes composed of 16 μmoles phosphatidylcholine (PC) or distearoyl phosphatidylcholine (DSPC), 8 μmoles of (dioleoyl phosphatidylethanolamine (DOPE) or cholesterol and 4 μmoles of the cationic lipid 1,2-dioleoyl-3-(trimethylammonium propane (DOTAP) (molar ratios 1:0.5:0.25). Incorporation efficiency was high (89-93% of the amount of DNA used) in all four formulations tested and incorporated DNA was shown to be resistant to displacement in the presence of the competing anionic sodium dodecyl sulfate mols. This is consistent with the notion that most of the DNA is incorporated within the multilamellar vesicles structure rather than being vesicle surface-complexed. Stability studies performed in simulated intestinal media also demonstrated that dehydration rehydration vesicles (DRV) incorporating DNA (DRV(DNA)) were able to retain significantly more of their DNA content compared to DNA complexed with preformed small unilamellar vesicles (SUV-DNA) of the same composition Moreover, after 4h incubation in the media, DNA loss for DSPC DRV(DNA) was only minimal, suggesting this to be the most stable formulation. Oral (intragastric) liposome-mediated DNA **immunization** studies employing a variety of DRV(DNA) formulations as well as naked DNA revealed that secreted IgA responses against the encoded HBsAg were (as early as three weeks after the first dose) substantially higher after dosing with 100 μg liposome-entrapped DNA compared to naked DNA. Throughout the fourteen week investigation, IgA responses in mice were consistently higher with the DSPC DRV(DNA) liposomes compared to naked DNA and correlated well with their improved DNA retention when exposed to model intestinal fluids. To investigate gene expression after oral (intragastric) administration, mice were given 100 μg of naked or DSPC DRV liposome-entrapped plasmid DNA

expressing the enhanced green fluorescent protein (pCMV.EGFP). Expression of the gene, in terms of fluorescence intensity in the draining mesenteric lymph nodes, was much greater in mice dosed with liposomal DNA than in animals dosed with the naked DNA. These results suggest that DSPC DRV liposomes containing DNA (Lipodine) may be a useful system for the oral delivery of DNA **vaccines.**

CC 63-3 (Pharmaceuticals)

ST liposome DNA **vaccine** oral

IT **Vaccines**
Zeta potential
(liposome-mediated DNA **vaccination** by oral route)

IT **DNA**
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(liposome-mediated DNA **vaccination** by oral route)

IT Phosphatidylcholines, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-mediated DNA **vaccination** by oral route)

IT **Drug delivery systems**
(liposomes; liposome-mediated DNA **vaccination** by **oral** route)

IT Gastric juice
(stability in gastric and intestinal media of liposome-DNA **vaccines**)

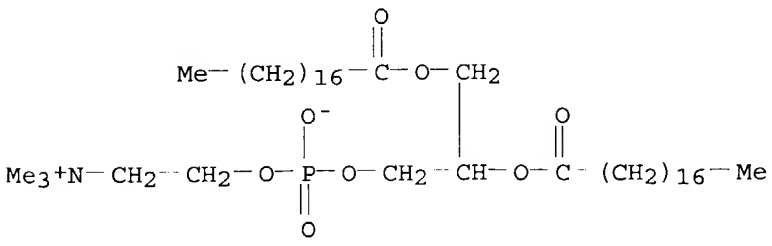
IT Intestinal juice
Stability
(stability in intestinal media of liposome-DNA **vaccines**)

IT 57-88-5, Cholesterol, biological studies 2462-63-7, Dioleoyl phosphatidylethanolamine **4539-70-2**, Distearoyl phosphatidylcholine **144189-73-1**, Dotap
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-mediated DNA **vaccination** by oral route)

IT **4539-70-2**, Distearoyl phosphatidylcholine **144189-73-1**, Dotap
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-mediated DNA **vaccination** by oral route)

RN 4539-70-2 HCAPLUS

CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 144189-73-1 HCAPLUS

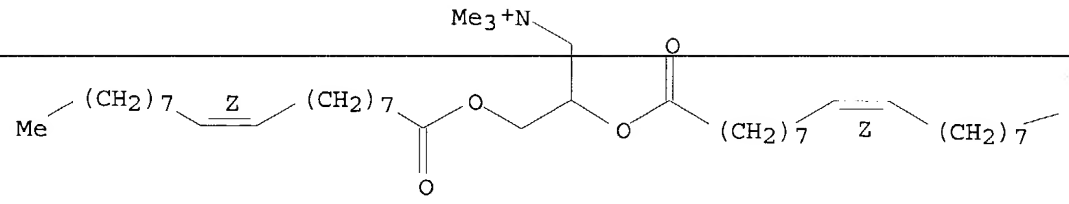
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO_3^-

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 14 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:657932 HCAPLUS
DOCUMENT NUMBER: 137:190751
TITLE: Amphoteric liposomes and their usage for the encapsulation of drugs and their transport into cells
INVENTOR(S): Panzner, Steffen; Fankhaenel, Stefan; Essler, Frank; Panzner, Cornelia
PATENT ASSIGNEE(S): Novosom A.-G., Germany
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002066012 A2 20020829 WO 2002-EP1880 20020221
WO 2002066012 A3 20021219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
DE 10109897 A1 20021107 DE 2001-10109897 20010221
US 2003099697 A1 20030529 US 2002-81617 20020221
EP 1363601 A2 20031126 EP 2002-701290 20020221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
BR 2002007775 A 20040330 BR 2002-7775 20020221
PRIORITY APPLN. INFO.: DE 2001-10109897 A 20010221
WO 2002-EP1880 W 20020221

AB The invention relates to amphoteric liposomes comprising pos. and neg. membrane-permeable or membrane-forming charge-carriers and to the use of the liposomes for the encapsulation of proteins, peptides, and nucleic acids. The liposomes are used to transport active substances into cells and to release them. Thus amphoteric liposomes with permanent neg. charge carriers and pos. chargable carriers were prepared from 5 mg histaminyl cholesterol hemisuccinate, 7.8 mg POPC and 2 mg DPPG. A lipid film of the liposomes was prepared and dissolved in a pH 7 buffer; 1 mM serum was added. The mixture was stirred for 15 min at 37°C; the mixture became uniformly turbid but no flocculation occurred.

IC ICM A61K009-127
CC 63-6 (Pharmaceuticals)
IT Blood serum
Drug delivery systems
Electric charge
Encapsulation
Isoelectric point
Particle size
Peritoneum
Zeta potential
pH
(amphoteric liposomes and usage for encapsulation of drugs and transport into cells)
IT **DNA**
Lipids, biological studies
Nucleic acids
Peptides, biological studies
Proteins
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amphoteric liposomes and usage for encapsulation of drugs and transport into cells)
IT Ceramides
Diglycerides
Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
RNA
Sphingolipids

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amphoteric liposomes and usage for encapsulation of drugs and transport into cells)

IT **Drug delivery systems**
(injections, i.v.; amphoteric liposomes and usage for encapsulation of drugs and transport into cells)

IT **Drug delivery systems**
(liposomes; amphoteric liposomes and usage for encapsulation of drugs and transport into cells)

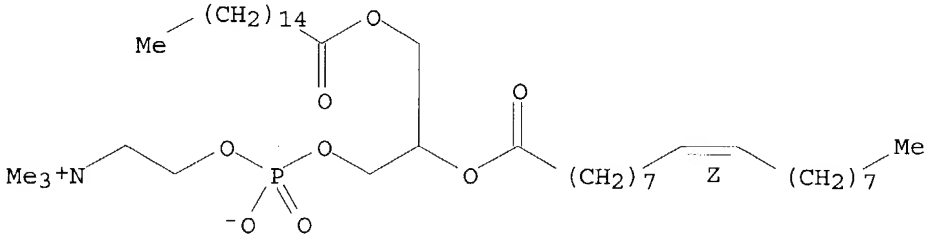
IT 4537-77-3, DPPG **26662-91-9**, 1-Palmitoyl-2-oleoyl-phosphatidylcholine 449791-79-1
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amphoteric liposomes and usage for encapsulation of drugs and transport into cells)

IT 57-88-5, Cholesterol, biological studies 1510-21-0, Cholesterol hemisuccinate **144189-73-1**, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amphoteric liposomes and usage for encapsulation of drugs and transport into cells)

IT **26662-91-9**, 1-Palmitoyl-2-oleoyl-phosphatidylcholine
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amphoteric liposomes and usage for encapsulation of drugs and transport into cells)

RN 26662-91-9 HCAPLUS
CN 3,5,8-Trioxa-4-phosphahexacos-17-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-9-oxo-7-[[(1-oxohexadecyl)oxy]methyl]-, inner salt, 4-oxide, (17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT **144189-73-1**, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amphoteric liposomes and usage for encapsulation of drugs and transport into cells)

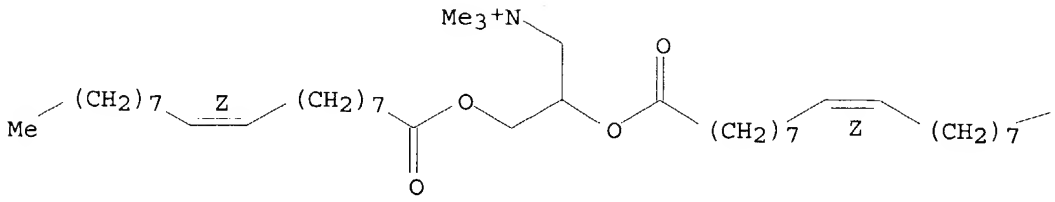
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO_3^-

L52 ANSWER 15 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:476451 HCAPLUS
DOCUMENT NUMBER: 138:243090
TITLE: Lipoplex-induced hemagglutination: potential involvement in intravenous gene delivery
AUTHOR(S): Eliyahu, H.; Servel, N.; Domb, A. J.; Barenholz, Y.
CORPORATE SOURCE: Department of Biochemistry, Hebrew University-Hadassah Medical School, Jerusalem, Israel
SOURCE: Gene Therapy (2002), 9(13), 850-858
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We report a study aiming to characterize the interaction of blood and blood components with lipoplexes under conditions relevant to in vivo i.v. transfection. In this study we focus on the interaction of lipoplexes with red blood cells (RBC). It was found that no significant hemolysis occurred during several hours' incubation using lipoplex compns. and lipoplex/red blood cell ratios in the range commonly used for in vivo transfection. However, the interaction of RBC with lipoplexes resulted in massive agglutination, which occurs irresp. of the type of cationic lipid or helper lipid. Agglutination was also induced by polyplexes (such as dendrimer/DNA complexes) and lipoplexes in the presence of spermidine or

protamine sulfate (the latter induced hemagglutination by itself). DSPE-PEG2000 inserted into the lipoplexes inhibits hemagglutination somewhat. In order to understand the effect of serum on the agglutination better, plasma was separated into its high mol. weight components (HMWC, >14 kDa) and its low mol. weight components (LMWC, ≤14 kDa). These fractions were characterized for their level of proteins, primary amino groups, osmotic pressure, and elec. conductivity, and compared with saline (0.15 M NaCl). It was found that both LMWC and HMWC inhibit agglutination by themselves, although whole serum demonstrates better hemagglutination inhibition than each fraction sep. The inhibitory effect of the serum (or plasma) is explained by its effect on the electrostatics of the lipoplexes, reducing their pos. charge, as was demonstrated using fluorescein-phosphatidylethanolamine-labeled lipoplexes. The effect of LMWC was related to ionic strength and was equal to the effect of 0.15 M NaCl. The level of agglutination was reduced with increasing lipoplex DNA-/cationic lipid+ (DNA-/L+) ratio. However, at the low DNA-/L+ ratio needed to achieve significant in vivo transfection after i.v. administration, massive agglutination occurred. These data suggest that i.v. administration of lipoplexes and polyplexes may lead to RBC agglutination, and the agglutinates formed may explain the localization of lipoplexes and expression of their transgenes in the lungs.

CC 63-6 (Pharmaceuticals)

IT **DNA**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(lipoplex-induced hemagglutination and potential involvement in i.v. gene delivery)

IT **Drug delivery systems**
(lipoplexes; lipoplex-induced hemagglutination and potential involvement in i.v. gene delivery)

IT 57-88-5, Cholesterol, biological studies 4004-05-1 **4235-95-4**, 1,2-Dioleoyl-sn-glycero-3-phosphatidylcholine **113669-21-9** **168479-03-6**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipoplex-induced hemagglutination and potential involvement in i.v. gene delivery)

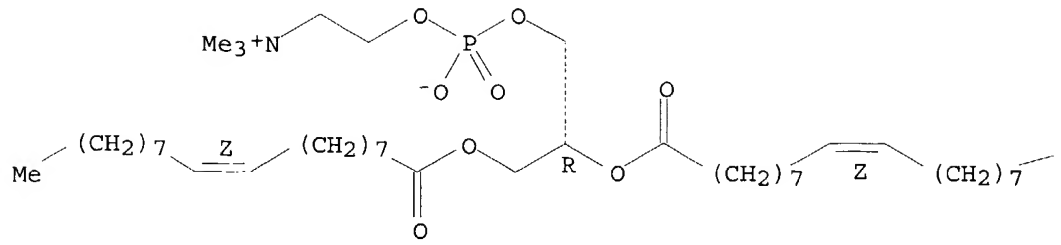
IT **4235-95-4**, 1,2-Dioleoyl-sn-glycero-3-phosphatidylcholine **113669-21-9** **168479-03-6**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipoplex-induced hemagglutination and potential involvement in i.v. gene delivery)

RN 4235-95-4 HCAPLUS

CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



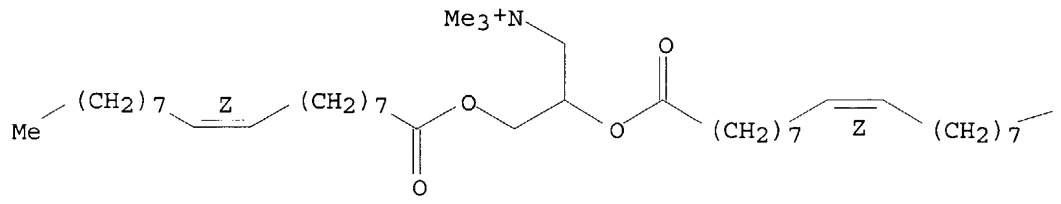
PAGE 1-B

Me

RN 113669-21-9 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

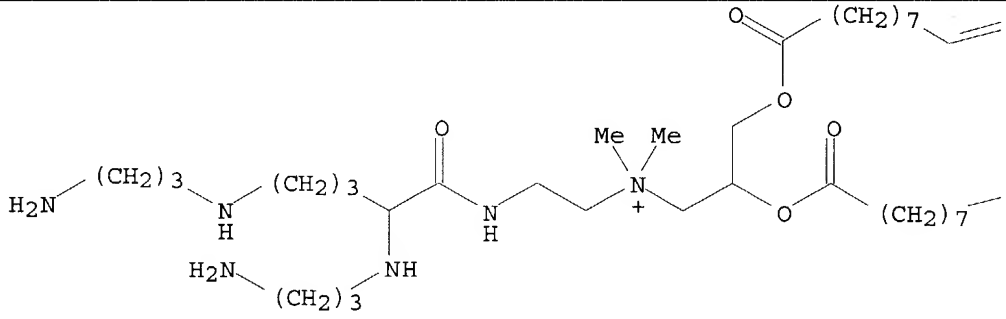
RN 168479-03-6 HCAPLUS
CN 1-Propanaminium, N-[2-[[2,5-bis[(3-aminopropyl)amino]-1-oxopentyl]amino]ethyl]-N,N-dimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, salt with trifluoroacetic acid (1:1) (9CI) (CA INDEX NAME)

CM 1

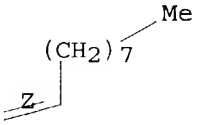
CRN 168479-02-5
CMF C54 H107 N6 O5

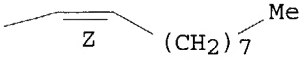
Double bond geometry as shown.

PAGE 1-A



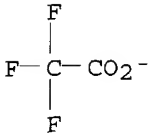
PAGE 1-B





CM 2

CRN 14477-72-6
CMF C2 F3 O2



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 16 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:332010 HCAPLUS
DOCUMENT NUMBER: 136:345764
TITLE: Lipid formulations for targeted delivery
INVENTOR(S): Cullis, Pieter R.; MacLachlan, Ian; Fenske, David B.
PATENT ASSIGNEE(S): The University of British Columbia, Can.; Inex Pharmaceuticals Corporation
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002034236	A2	20020502	WO 2001-CA1513	20011025
WO 2002034236	A3	20030109		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002014854	A5	20020506	AU 2002-14854	20011025
EP 1328254	A2	20030723	EP 2001-983342	20011025
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511572	T2	20040415	JP 2002-537290	20011025

PRIORITY APPLN. INFO.: US 2000-243185P P 20001025
WO 2001-CA1513 W 20011025

AB The present invention provides lipid-based systemic delivery vehicles and method for selectively targeting an active agent to a specific tissue site. The methods include designing a lipid-based systemic delivery vehicle having a plurality of constituent parts, and thereafter varying the amts. of each of the plurality of constituent parts to impart tissue selectivity. After tissue selectivity is imparted it is possible to selectively target an active agent to a specific tissue site.

IC ICM A61K009-127
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1
IT Antitumor agents
Drug delivery systems
Gene therapy
Molecular weight distribution
Mus
Plasmid vectors
Stabilizing agents
Transformation, genetic
(lipid formulations for targeted delivery)
IT **Antisense oligonucleotides**
Ribozymes
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC

(Process); USES (Uses)
(lipid formulations for targeted delivery)

IT Ceramides
Nucleic acids
Phosphatidylcholines, biological studies
Polyoxyalkylenes, biological studies
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid formulations for targeted delivery)

IT **Drug delivery systems**
(liposomes; lipid formulations for targeted delivery)

IT **Drug delivery systems**
(targeted; lipid formulations for targeted delivery)

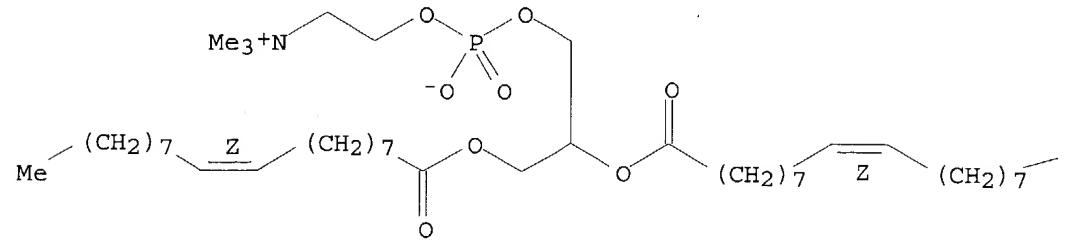
IT 2462-63-7, Dope 3700-67-2, DDAB 7212-69-3, Dodac 25322-68-3, Polyethylene glycol **68737-67-7**, Dioleoyl phosphatidyl choline **104162-48-3**, Dotma **144189-73-1**, Dotap
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid formulations for targeted delivery)

IT **68737-67-7**, Dioleoyl phosphatidyl choline **104162-48-3**, Dotma **144189-73-1**, Dotap
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid formulations for targeted delivery)

RN 68737-67-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (18Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



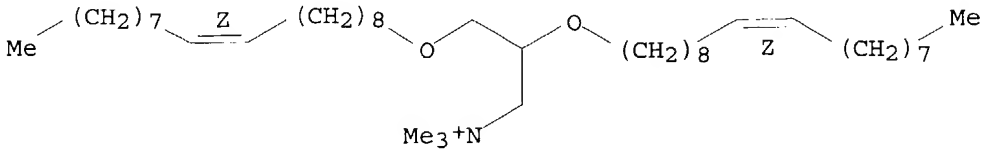
PAGE 1-B

Me

RN 104162-48-3 HCAPLUS

CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



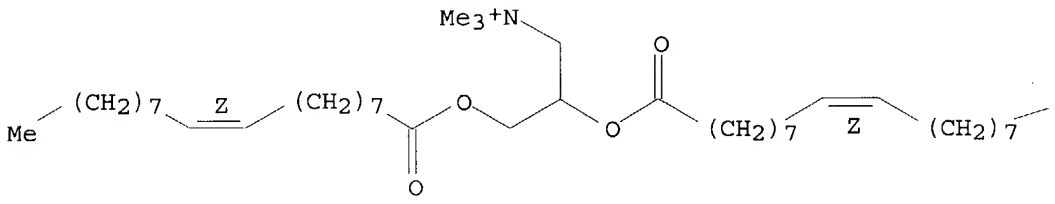
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

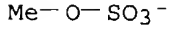
PAGE 1-A



PAGE 1-B

CM 2

CRN 21228-90-0
CMF C H3 O4 S



L52 ANSWER 17 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:314746 HCAPLUS
DOCUMENT NUMBER: 136:330564
TITLE: Lipid-protein-sugar microparticles for drug delivery
INVENTOR(S): Kohane, Daniel S.; Lipp, Michael M.; Langer, Robert S.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032398	A2	20020425	WO 2001-US32378	20011016
WO 2002032398	A3	20030109		
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
US 2002150621	A1	20021017	US 2001-981020	20011016

PRIORITY APPLN. INFO.: US 2000-240636P P 20001016

AB Lipid-protein-sugar microparticles (LPSPs) are provided as a vehicle for drug delivery. Any therapeutic, diagnostic, or prophylactic agent may be encapsulated in a lipid-protein-sugar matrix to form microparticles. Preferably the diameter of the LPSP ranges from 50 to 10 μm. The particles may be prepared by using any known lipid (e.g., DPPC), protein (e.g., albumin), or sugar (e.g., lactose). Methods of preparing and administering the particles are also provided. Methods of providing a nerve block are also provided by administering LPSPs with a local anesthetic (e.g., bupivacaine) within the vicinity of a nerve. Title microparticles (DPPC-albumin-lactose) were prepared containing bupivacaine. The drug release from the particles was complete within 24 h.

IC ICM A61K009-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT Anticonvulsants
Biocompatibility
Drug delivery systems
Emulsifying agents
Human
Nerve
Particle size distribution
Solubilization
Surfactants
Vasodilators
(lipid-protein-sugar microparticles for drug delivery)
IT Albumins, biological studies
Antibodies and Immunoglobulins
Antigens
Carbohydrates, biological studies
Cardiolipins
Cerebrosides
Enzymes, biological studies
Fatty acids, biological studies
Glycerides, biological studies

Glycerophospholipids
Glycosaminoglycans, biological studies
Lecithins
Lipids, biological studies
Lysophosphatidylcholines
Phosphatidic acids
Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphatidylinositols
Phosphatidylserines
Phospholipids, biological studies
Polymers, biological studies
Polyoxyalkylenes, biological studies
Proteins
Sialic acids
Sphingomyelins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid-protein-sugar microparticles for drug delivery)

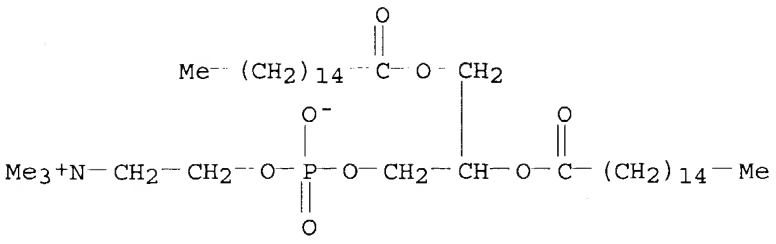
IT **Drug delivery systems**
(microparticles, controlled-release; lipid-protein-sugar microparticles for drug delivery)

IT **Drug delivery systems**
(microparticles; lipid-protein-sugar microparticles for drug delivery)

IT 50-99-7, Glucose, biological studies 57-10-3, Palmitic acid, biological studies 57-48-7, Fructose, biological studies 57-88-5, Cholesterol, biological studies 57-88-5D, Cholesterol, esters 58-86-6, Xylose, biological studies 59-23-4, Galactose, biological studies 59-46-1, Procaine 63-42-3, Lactose 69-65-8, Mannitol 69-79-4, Maltose 85-79-0, Dibucaine 94-24-6, Tetracaine 96-88-8, Mepivacaine 110-27-0, Isopropyl myristate 112-80-1, Oleic acid, biological studies 124-22-1, Dodecylamine 124-30-1, Stearylamine 137-58-6, Lidocaine 143-27-1, Hexadecylamine 512-69-6, Raffinose 1190-63-2, Hexadecyl stearate 1323-38-2, Glyceryl ricinoleate 2197-63-9, Dicetyl phosphate 2462-63-7, DOPE **2644-64-6**, DPPC 2763-96-4, Muscimol 4537-77-3, DPPG 9001-37-0, Glucose oxidase 9002-89-5, Poly(vinyl alcohol) 9002-92-0, Polyethylene glycol lauryl ether 9004-10-8, Insulin, biological studies 9004-32-4, Carboxymethyl cellulose 9004-34-6, Cellulose, biological studies 9004-53-9, Dextrin 9004-54-0, Dextran, biological studies 9004-54-0D, Dextran, derivs. 9004-61-9, Hyaluronic acid 9004-67-5, Methyl Cellulose 9005-25-8, Starch, biological studies 9007-28-7, Chondroitin sulfate 9012-76-4, Chitosan 18010-40-7, Bupivacaine hydrochloride 21829-25-4, Nifedipine 23964-58-1, Articaine 24730-31-2, Surfactin 25301-02-4, Tyloxapol 25322-68-3, Polyethylene glycol 25322-68-3D, Polyethylene glycol, phosphatidylethanolamine conjugates 26266-58-0, Span 85 36653-82-4, Hexadecanol 64044-51-5, Lactose monohydrate **68737-67-7**, DOPC **104162-48-3**, DOTMA 106392-12-5, Poloxamer
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid-protein-sugar microparticles for drug delivery)

IT **2644-64-6**, DPPC **68737-67-7**, DOPC **104162-48-3**, DOTMA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid-protein-sugar microparticles for drug delivery)

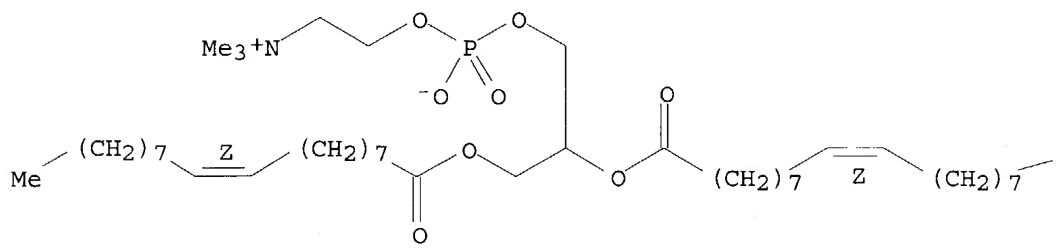
RN 2644-64-6 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 68737-67-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (18Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

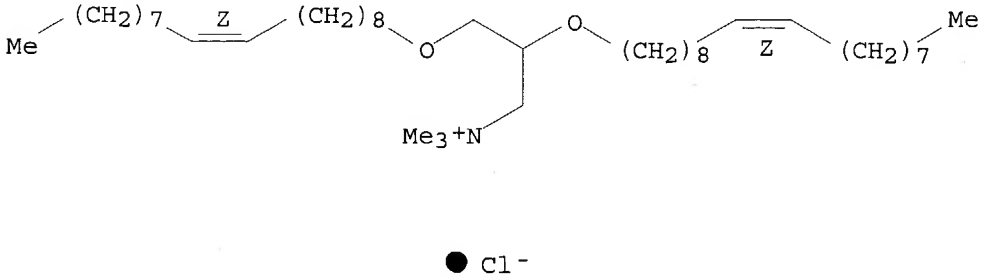
PAGE 1-A



PAGE 1-B

RN 104162-48-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L52 ANSWER 18 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:314744 HCAPLUS
DOCUMENT NUMBER: 136:330527
TITLE: Lipid-protein-sugar particles for delivery of nucleic acids
INVENTOR(S): Kohane, Daniel S.; Anderson, Daniel G.; Langer, Robert S.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032396	A2	20020425	WO 2001-US32210	20011016
WO 2002032396	A3	20030206		
WO 2002032396	C2	20030717		
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
US 2002150626	A1	20021017	US 2001-981460	20011016

PRIORITY APPLN. INFO.: US 2000-240698P P 20001016

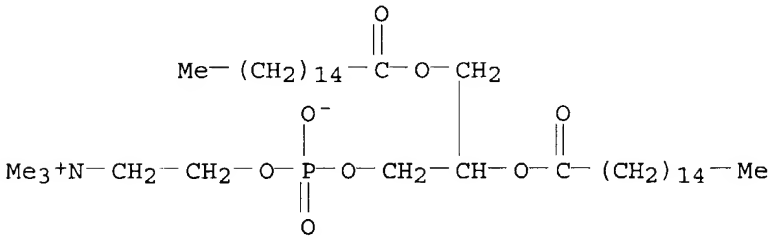
AB Lipid-protein-sugar particles (LPSPs) are provided as a vehicle for the delivery of nucleic acids. Any polynucleotide (e.g., DNA, RNA) may be encapsulated in a lipid-protein-sugar matrix to form microparticles. Preferably the diameter of the LPSP ranges from 50 nm to 10 μm. The particles may be prepared using any known lipid (e.g., DPPC), protein (e.g., albumin), or sugar (e.g., lactose). Methods of preparing the particles and administering the particles for gene therapy are also provided. Preferably the methods of preparing the LPSPs do not significantly damage the polynucleotide to be delivered.

IC ICM A61K009-00
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 15
IT **Antigens**
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(bacterial; lipid-protein-sugar particles for delivery of nucleic acids)
IT **Drug delivery systems**
(inhalants; lipid-protein-sugar particles for delivery of nucleic acids)
IT **Drug delivery systems**
(injections; lipid-protein-sugar particles for delivery of nucleic acids)
IT **Drug delivery systems**
Emulsifying agents
Gene therapy
Genetic vectors
Hematopoietic precursor cell
Particle size
Plasmid vectors
Surfactants

(lipid-protein-sugar particles for delivery of nucleic acids)
IT Albumins, biological studies
Antibodies and Immunoglobulins
Carbohydrates, biological studies
Cardiolipins
Cardiolipins
Cerebrosides
DNA
Diglycerides
Enzymes, biological studies
Fatty acids, biological studies
Glycosaminoglycans, biological studies
Lecithins
Lipids, biological studies
Lysophosphatidylcholines
Phosphatidic acids
Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphatidylinositols
Phosphatidylserines
Phospholipids, biological studies
Polymers, biological studies
Polynucleotides
Polyoxyalkylenes, biological studies
Proteins
RNA
Sialic acids
Sphingomyelins
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid-protein-sugar particles for delivery of nucleic acids)
IT **Drug delivery systems**
(microparticles; lipid-protein-sugar particles for delivery of nucleic acids)
IT 57-10-3, Palmitic acid, biological studies 57-48-7, Fructose, biological studies 57-88-5, Cholesterol, biological studies 57-88-5D, Cholesterol, esters 58-86-6, Xylose, biological studies 63-42-3, Lactose 69-65-8, Mannitol 69-79-4, Maltose 110-15-6D, Succinic acid, glycerides 110-27-0, Isopropyl myristate 112-80-1, Oleic acid, biological studies 124-22-1, Dodecylamine 124-30-1, Stearylamine 143-27-1, Hexadecylamine 475-31-0 512-69-6, Raffinose 629-70-9, Palmityl Acetate 1190-63-2, Hexadecyl stearate 2197-63-9, Dicetylphosphate 2462-63-7, Dope **2644-64-6**, Dipalmitoylphosphatidylcholine 4537-77-3, Dipalmitoylphosphatidylglycerol 9000-11-7, Carboxymethyl cellulose 9001-37-0, Glucose oxidase 9002-92-0 9004-34-6, Cellulose, biological studies 9004-53-9, Dextrin 9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid 9004-67-5, Methyl cellulose 9005-25-8, Starch, biological studies 9007-28-7, Chondroitin sulfate 9012-76-4, Chitosan 24730-31-2, Surfactin 25301-02-4, Tyloxapol 25322-68-3, Polyethylene glycol 26266-58-0, Span 85 51260-59-4, Hexadecanol 58561-47-0 **68737-67-7**, Dioleoylphosphatidylcholine **104162-48-3**, Dotma
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid-protein-sugar particles for delivery of nucleic acids)
IT **2644-64-6**, Dipalmitoylphosphatidylcholine **68737-67-7**,

Dioleoylphosphatidylcholine **104162-48-3**, Dotma
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid-protein-sugar particles for delivery of nucleic acids)

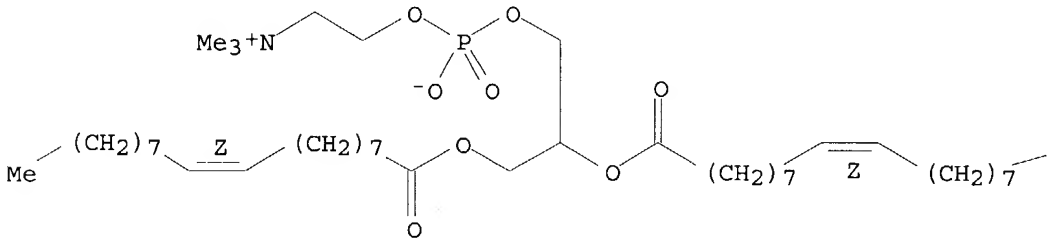
RN 2644-64-6 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 68737-67-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (18Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

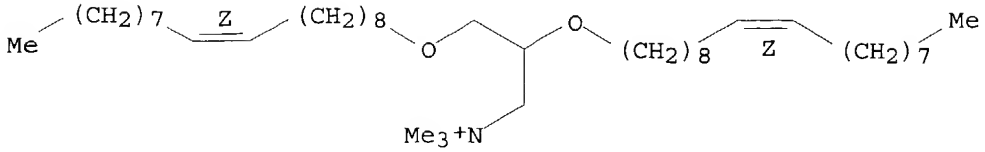


PAGE 1-B

Me

RN 104162-48-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● Cl⁻

L52 ANSWER 19 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:275821 HCAPLUS
DOCUMENT NUMBER: 136:308524
TITLE: Non-pathogenic bacterium-derived Kyberdrug as auto-**vaccines** with immune-regulating effects
INVENTOR(S): Paradies, H. Henrich; Rusch, Volker; Zimmermann, Kurt
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028424	A2	20020411	WO 2001-IB2284	20011005
WO 2002028424	A3	20021107		
WO 2002028424	C2	20030912		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002023970	A5	20020415	AU 2002-23970	20011005
US 2002155997	A1	20021024	US 2001-971557	20011005
EP 1341546	A2	20030910	EP 2001-986266	20011005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004510746	T2	20040408	JP 2002-532248	20011005

PRIORITY APPLN. INFO.:
US 2000-238656P P 20001006
US 2001-263494P P 20010123
WO 2001-IB2284 W 20011005

AB The present invention is directed to a "Kyberdrug" and to a pharmaceutical composition containing an effective amount of the Kyberdrug and a pharmaceutical carrier therefor, and its medicinal use as an immune modulating drug exhibiting auto-**vaccine**-like activities. The kyberdrugs are free of enterotoxin, endotoxin, and verotoxin and are purified from non-pathogenic bacterium such as enterobacteriaceae, especially Escherichia coli, found in mammals including humans with acute or chronic infections

of bacterial or viral origin. These kyberdrugs are useful for treating bacterial or viral infections in humans.

IC ICM A61K039-02

CC 15-2 (Immunochemistry)
Section cross-reference(s): 9, 10, 63

ST kyberdrug nonpathogenic bacterium enterobacteriaceae mammal human; **vaccine** kyberdrug enterobacteriaceae bacterial viral infection

IT **Vaccines**
(auto-; non-pathogenic bacterium or Enterobacteriaceae-derived kyberdrugs as autovaccines with immune-regulating effects)

IT 50-99-7, Glucose, biological studies 56-87-1, L-Lysine, biological studies 59-23-4, Galactose, biological studies 546-46-3, Zinc citrate 1961-72-4, 3-Hydroxytetradecanoic acid 3329-30-4, N-Methylglucosamine 4468-02-4, Zinc gluconate 7439-95-4D, Magnesium, salts 7440-66-6D, Zinc, salts 7440-70-2D, Calcium, salts 7646-85-7, Zinc chloride, biological studies 14000-31-8, Pyrophosphate 16283-36-6, Zinc salicylate 25104-18-1, Poly-L-lysine 38000-06-5, Poly-L-lysine 51822-75-4 **68737-67-7**, Dioleoylphosphatidylcholine **144189-73-1** 149265-27-0 408512-46-9
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(non-pathogenic bacterium or Enterobacteriaceae-derived kyberdrugs as autovaccines with immune-regulating effects)

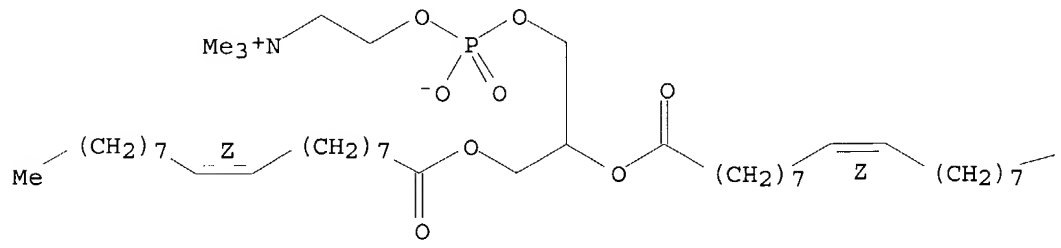
IT **68737-67-7**, Dioleoylphosphatidylcholine **144189-73-1**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(non-pathogenic bacterium or Enterobacteriaceae-derived kyberdrugs as autovaccines with immune-regulating effects)

RN 68737-67-7 HCAPLUS

CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (18Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

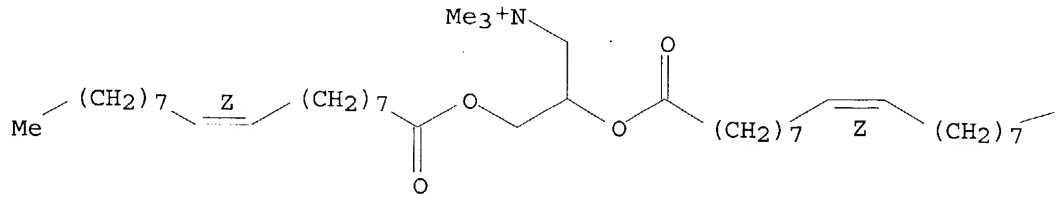
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO3-

L52 ANSWER 20 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:51238 HCAPLUS
DOCUMENT NUMBER: 136:123632
TITLE: Drug delivery formulations and targeting comprising cationic liposomes
INVENTOR(S): Campbell, Robert B.; Brown, Edward B.; Fukumura, Dai; Jain, Rakesh K.
PATENT ASSIGNEE(S): The General Hospital Corporation, USA
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003959	A1	20020117	WO 2001-US21183	20010705
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002090392	A1	20020711	US 2001-898107	20010703
US 6680068	B2	20040120		

PRIORITY APPLN. INFO.: US 2000-216173P P 20000706

AB The invention is based on the discovery that angiogenic vessels have heterogeneous surface charge and that cationic liposomes actually target human tumor blood vessels only in irregularly shaped patches. The invention thus features methods for delivering therapeutic compds. to angiogenic vascular endothelial surfaces using a mixture, or "cocktail", of pos. charged and neutral liposomes. The new methods can be used to target multiple regions on the same tumor vessel and/or clusters of vessels within the same tumor. Liposomes with different chemical and/or phys. properties (e.g., charge, stability, solubility, diameter) can be delivered simultaneously, and can target tumor vessels and other angiogenic vessels with greater efficiency compared to cationic liposomes alone. Liposomes comprising dioleoylphosphatidylcholine:cholesterol:dioleyltrimethylammoniu m propane:polyethylene glycol (35:10:50:5) were prepared The liposomes were passed through 100 nm filter membrane and cationic and neutral liposomes were combined in a 50:50 ratio to yield the desired charge ratio. When liposomes were injected to tumor-bearing mice. Tumors preferentially took up cationic liposomes.

IC ICM A61K009-127

CC 63-6 (Pharmaceuticals)

IT **Drug delivery systems**
(injections, i.v.; drug delivery formulations and targeting comprising cationic liposomes)

IT **Drug delivery systems**
(liposomes; drug delivery formulations and targeting comprising cationic liposomes)

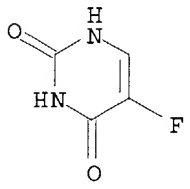
IT **Drug delivery systems**
(nasal; drug delivery formulations and targeting comprising cationic liposomes)

IT 50-18-0, Cyclophosphamide 50-44-2, Mercaptopurine 50-76-0, Dactinomycin **51-21-8**, Fluorouracil 52-24-4, Thiotepa 53-19-0, Mitotane 55-86-7, Mechlorethamine hydrochloride 55-98-1, Busulfan 57-22-7, Vincristine 57-88-5, Cholesterol, biological studies 59-05-2, Methotrexate 127-07-1, Hydroxyurea 147-94-4, Cytarabine 148-82-3, Melphalan **154-42-7**, Thioguanine 154-93-8, Carmustine 302-79-4, Tretinoin 305-03-3, Chlorambucil 320-67-2, Azacitidine 671-16-9, Procarbazine 865-21-4, Vinblastine 1404-00-8, Mitomycin **2644-64-6**, Dipalmitoylphosphatidylcholine 3700-67-2, Dimethyldioctadecylammonium bromide 3778-73-2, Ifosfamide **4235-95-4** 4291-63-8, Cladribine 4342-03-4, Dacarbazine **4539-70-2**, Distearoylphosphatidylcholine 7212-69-3 9015-68-3, Asparaginase 11056-06-7, Bleomycin 13010-47-4, Lomustine 15663-27-1, Cisplatin 18378-89-7, Plicamycin **18656-38-7**,

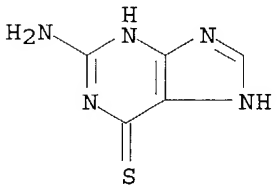
Dimyristoylphosphatidylcholine 18883-66-4, Streptozocin 20830-81-3, Daunorubicin 21679-14-1, Fludarabine 25322-68-3, Polyethyleneglycol 33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4, Carboplatin 51264-14-3, Amsacrine 58957-92-9, Idarubicin 65271-80-9, Mitoxantrone **68737-67-7**, Dioleoylphosphatidylcholine 71486-22-1, Vinorelbine **113669-21-9** 114977-28-5, Docetaxel 123948-87-8, Topotecan 127512-29-2 **132172-61-3** **153312-64-2** **168479-03-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery formulations and targeting comprising cationic liposomes)

IT **51-21-8**, Fluorouracil **154-42-7**, Thioguanine **2644-64-6**, Dipalmitoylphosphatidylcholine **4235-95-4** **4539-70-2**, Distearoylphosphatidylcholine **18656-38-7**, Dimyristoylphosphatidylcholine **68737-67-7**, Dioleoylphosphatidylcholine **113669-21-9** **132172-61-3** **153312-64-2** **168479-03-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery formulations and targeting comprising cationic liposomes)

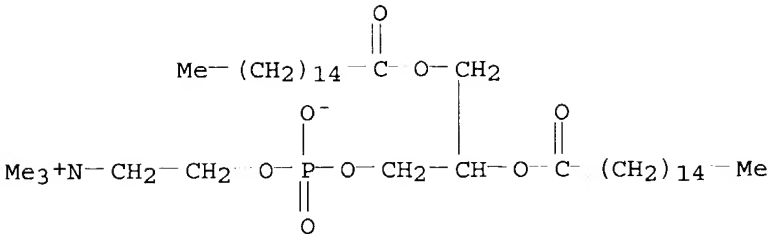
RN 51-21-8 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-fluoro- (9CI) (CA INDEX NAME)



RN 154-42-7 HCAPLUS
CN 6H-Purine-6-thione, 2-amino-1,7-dihydro- (9CI) (CA INDEX NAME)



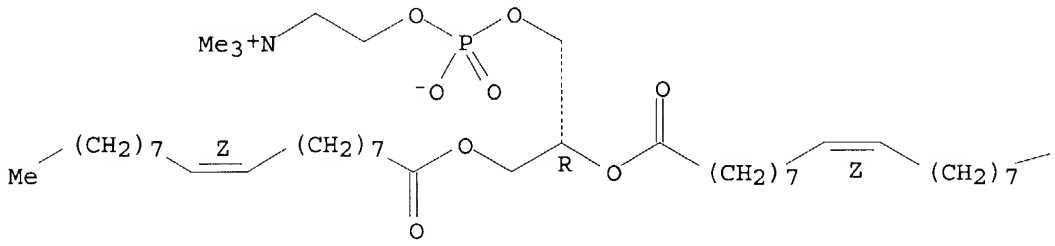
RN 2644-64-6 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 4235-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

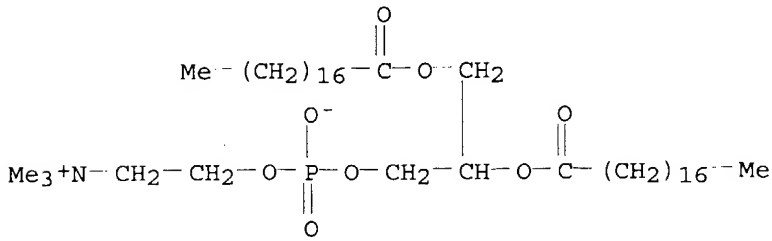
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A

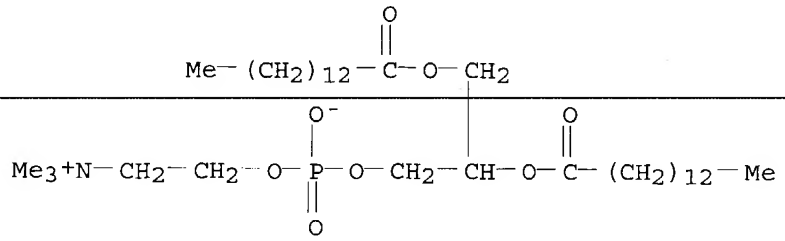


PAGE 1-B

RN 4539-70-2 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



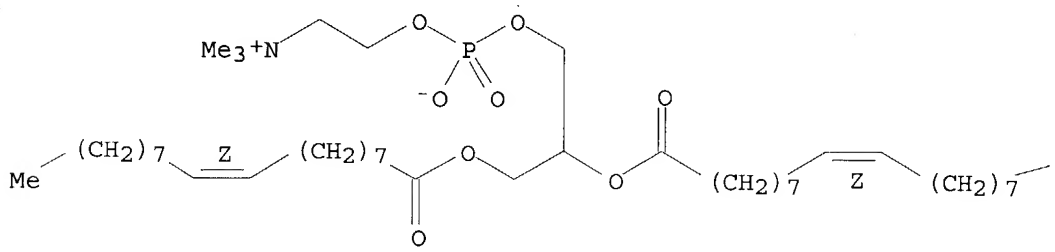
RN 18656-38-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatricosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxotetradecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 68737-67-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (18Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



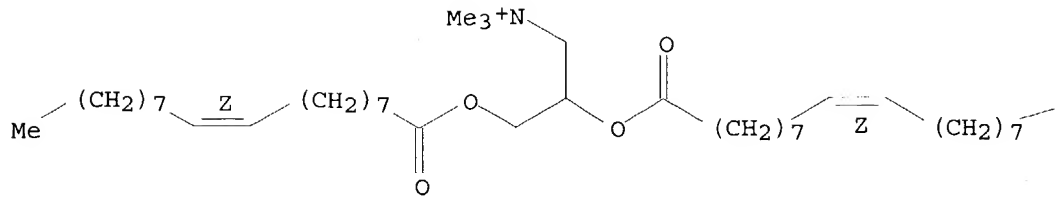
PAGE 1-B

Me

RN 113669-21-9 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



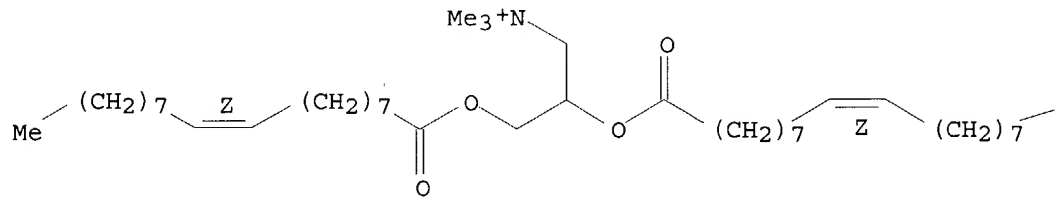
PAGE 1-B

Me

RN 132172-61-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

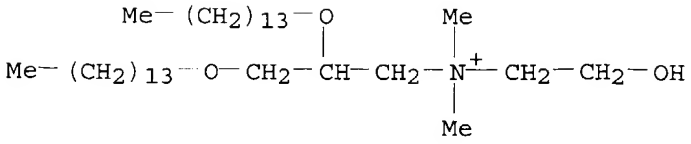
PAGE 1-A



PAGE 1-B

Me

RN 153312-64-2 HCAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



● Br^-

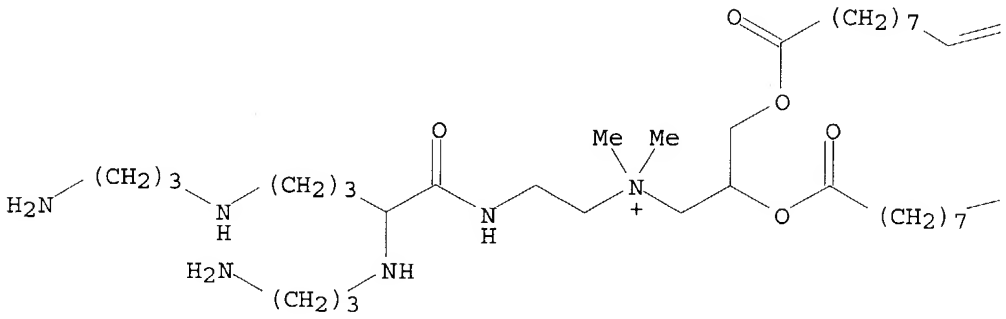
RN 168479-03-6 HCAPLUS
CN 1-Propanaminium, N-[2-[[2,5-bis[(3-aminopropyl)amino]-1-oxopentyl]amino]ethyl]-N,N-dimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, salt with trifluoroacetic acid (1:1) (9CI) (CA INDEX NAME)

CM 1

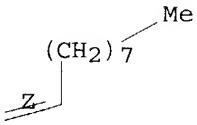
CRN 168479-02-5
CMF C54 H107 N6 O5

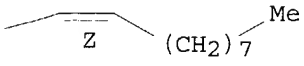
Double bond geometry as shown.

PAGE 1-A



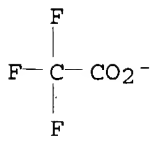
PAGE 1-B





CM 2

CRN 14477-72-6
CMF C2 F3 O2



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 21 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:833064 HCAPLUS
DOCUMENT NUMBER: 135:352781
TITLE: Compositions and methods for protecting cells during cancer chemotherapy and radiotherapy
INVENTOR(S): Fahl, William E.; Raghavachari, Nalimi; Zhu, Ming; Kink, John
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085142	A1	20011115	WO 2001-US14464	20010504
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1280556	A1	20030205	EP 2001-933017	20010504
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004515453	T2	20040527	JP 2001-581796	20010504

PRIORITY APPLN. INFO.: US 2000-565714 A 20000505
WO 2001-US14464 W 20010504

AB Compns., pharmaceutical prepns. and methods are disclosed for protecting non-neoplastic cells from damage caused by cancer chemotherapeutic agents or radiation therapy, during the course of cancer therapy or bone marrow transplant. These are based on the use of chemoprotective inducing agents that induce or increase production of cellular detoxification enzymes in target cell populations. The compns. and methods are useful to reduce or prevent hair loss, gastrointestinal distress and lesions of the skin and

oral mucosa that commonly occur in patients undergoing cancer therapy. Also disclosed is a novel assay system for identifying new chemoprotective inducing agents.

IC ICM A61K009-27
ICS A61K047-00; A61L015-16; A61K009-66; A61K009-20

CC 1-6 (Pharmacology)
Section cross-reference(s): 8, 63

IT Alopecia
Antitumor agents
Cytoprotective agents
Drug delivery systems
Radioprotectants
Radiotherapy
(compns. and methods for protecting cells during cancer chemotherapy and radiotherapy)

IT **Drug delivery systems**
(emulsions; compns. and methods for protecting cells during cancer chemotherapy and radiotherapy)

IT **Drug delivery systems**
(injections; compns. and methods for protecting cells during cancer chemotherapy and radiotherapy)

IT **Drug delivery systems**
(liposomes; compns. and methods for protecting cells during cancer chemotherapy and radiotherapy)

IT **Drug delivery systems**
(microparticles; compns. and methods for protecting cells during cancer chemotherapy and radiotherapy)

IT **Drug delivery systems**
(nasal; compns. and methods for protecting cells during cancer chemotherapy and radiotherapy)

IT **Drug delivery systems**
(**oral**; compns. and methods for protecting cells during cancer chemotherapy and radiotherapy)

IT **DNA**
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(plasmid, in liposomal formulations; compns. and methods for protecting cells during cancer chemotherapy and radiotherapy)

IT **Drug delivery systems**
(rectal; compns. and methods for protecting cells during cancer chemotherapy and radiotherapy)

IT **Drug delivery systems**
(suspensions; compns. and methods for protecting cells during cancer chemotherapy and radiotherapy)

IT **Drug delivery systems**
(topical; compns. and methods for protecting cells during cancer chemotherapy and radiotherapy)

IT **Drug delivery systems**
(vaginal; compns. and methods for protecting cells during cancer chemotherapy and radiotherapy)

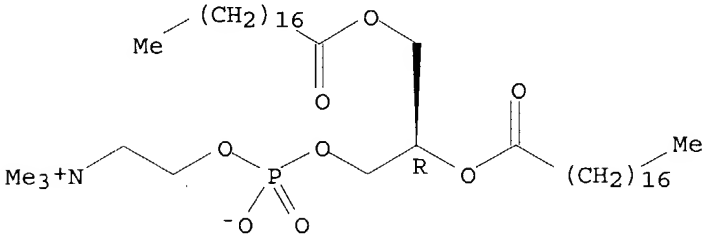
IT 57-55-6, Propylene glycol, biological studies 57-88-5, Cholesterol, biological studies 59-02-9, α-Tocopherol 64-17-5, Ethanol, biological studies 108-05-4, Vinyl acetate, biological studies **816-94-4**, DSPC 2462-63-7, DOPE **4235-95-4** 9003-39-8, PVP 9005-00-9, Polyoxyethylene stearyl ether 25322-68-3 27638-00-2, Glyceryl dilaurate 108032-13-9 127640-49-7 **144189-73-1**, DOTAP 294868-36-3
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(in liposomal formulations; compns. and methods for protecting cells during cancer chemotherapy and radiotherapy)

IT **816-94-4**, DSPC **4235-95-4 144189-73-1**, DOTAP
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in liposomal formulations; compns. and methods for protecting cells during cancer chemotherapy and radiotherapy)

RN 816-94-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

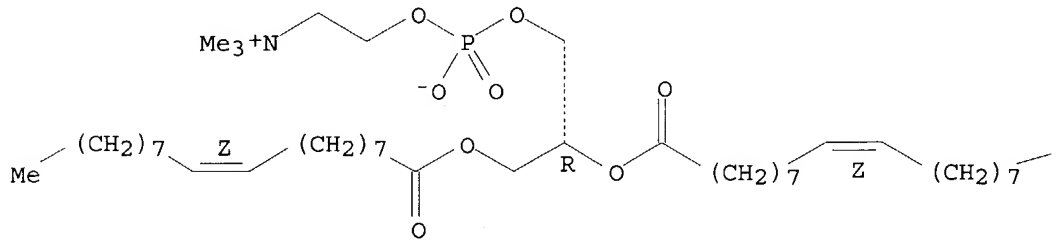
Absolute stereochemistry.



RN 4235-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

RN 144189-73-1 HCAPLUS

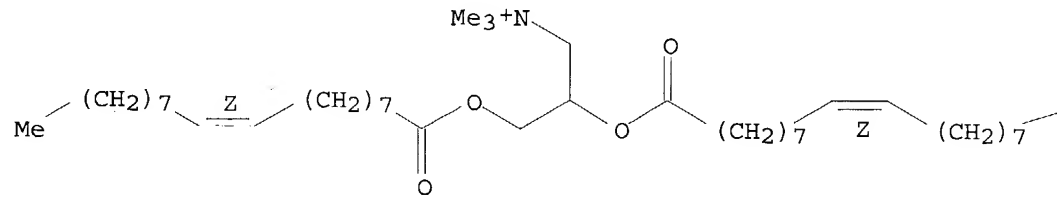
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me-O-SO3-

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 22 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:798087 HCAPLUS
DOCUMENT NUMBER: 135:348867
TITLE: Methods of enhancing SPLP-mediated transfection using endosomal membrane destabilizers
INVENTOR(S): Lam, Angela M. I.; Palmer, Lorne R.; Cullis, Pieter R.
PATENT ASSIGNEE(S): University of British Columbia, Can.
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001080900	A2	20011101	WO 2001-CA555	20010420
WO 2001080900	A3	20030424		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

WO 2000062813	A2	20001026	WO 2000-CA451	20000420
WO 2000062813	A3	20010809		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1355670	A2	20031029	EP 2001-927519	20010420

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004508012	T2	20040318	JP 2001-577996	20010420

PRIORITY APPLN. INFO.:

US 2000-553639	A	20000420
WO 2000-CA451	W	20000420
US 2000-227949P	P	20000825
US 1999-130151P	P	19990420
WO 2001-CA555	W	20010420

OTHER SOURCE(S): MARPAT 135:348867

AB The present invention provides novel and surprisingly effective methods for delivering nucleic acids to cells. These methods are based upon the discovery that the presence of endosomal membrane destabilizers (e.g., calcium) leads to a dramatic increase in the transfection efficiency of plasmids formulated as SPLP, or "stabilized plasmid-lipid particles.".

IC ICM A61K047-48

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 3

IT Chelation
Drug delivery systems
Endocytosis
Genetic vectors
Membrane, biological
Molecular weight distribution
Plasmid vectors
Plasmids
Transformation, genetic
pH
(enhancing SPLP-mediated transfection using endosomal membrane destabilizers)

IT **Nucleic acids**
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(enhancing SPLP-mediated transfection using endosomal membrane destabilizers)

IT **Antisense oligonucleotides**
Phosphatidylcholines, biological studies
Polyesters, biological studies
Ribozymes
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enhancing SPLP-mediated transfection using endosomal membrane destabilizers)

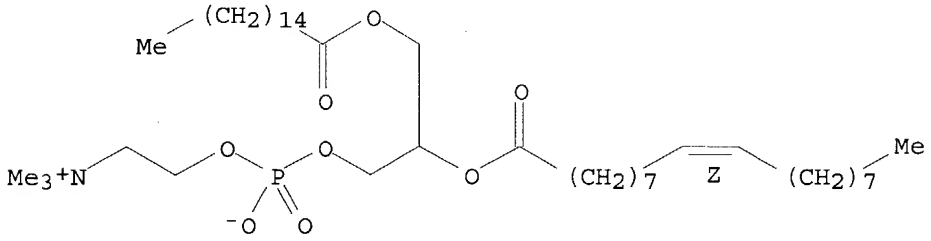
IT **Drug delivery systems**
(liposomes; enhancing SPLP-mediated transfection using endosomal membrane destabilizers)

IT 7212-69-3, Dodac 25322-68-3D, Polyethylene glycol, conjugates 26009-03-0D, Polyglycolic acid, conjugates 26023-30-3D, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)], conjugates 26100-51-6D, Polylactic acid, conjugates 26124-68-5D, Polyglycolic acid, conjugates **26662-91-9**, Popc 34346-01-5D, Glycolic acid-lactic acid copolymer, conjugates **104162-48-3**, Dotma 127512-29-2 **144189-73-1**, Dotap
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enhancing SPLP-mediated transfection using endosomal membrane destabilizers)

IT **26662-91-9**, Popc **104162-48-3**, Dotma **144189-73-1**
, Dotap
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enhancing SPLP-mediated transfection using endosomal membrane destabilizers)

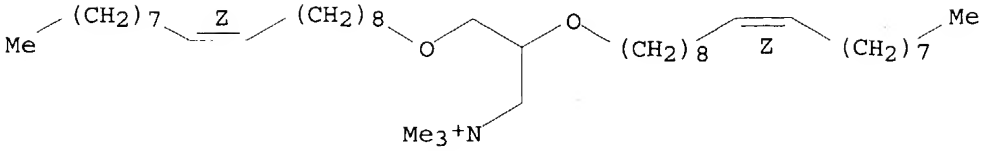
RN 26662-91-9 HCAPLUS
CN 3,5,8-Trioxa-4-phosphahexacos-17-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-9-oxo-7-[[(1-oxohexadecyl)oxy]methyl]-, inner salt, 4-oxide, (17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 104162-48-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



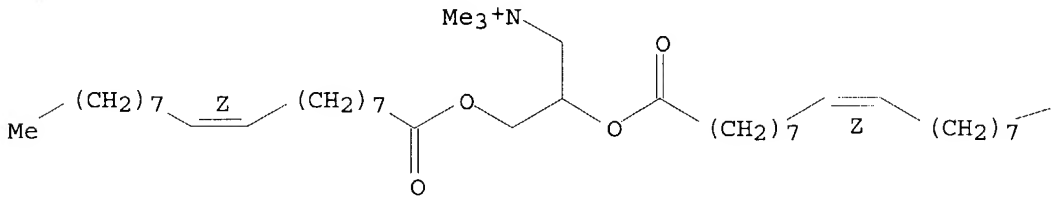
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

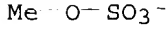
PAGE 1-A



PAGE 1-B

CM 2

CRN 21228-90-0
CMF C H3 O4 S



L52 ANSWER 23 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:781076 HCAPLUS
DOCUMENT NUMBER: 135:340281
TITLE: Gene inactivation by targeted DNA methylation using a m5C methylated oligonucleotide containing an imprinting element and a guiding element
PATENT ASSIGNEE(S): Genmethrax, Inc., USA; Board of Trustees of the Leland Stanford Junior University
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079441	A2	20011025	WO 2001-US10531	20010330
WO 2001079441	A3	20020228		
WO 2001079441	C2	20021227		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
AU 2001051208	A5	20011030	AU 2001-51208	20010330

PRIORITY APPLN. INFO.:
US 2000-196749P P 20000412
US 2000-214148P P 20000626
WO 2001-US10531 W 20010330

AB The invention provides methods and compns. related to polynucleotides that induce methylation at a target nucleotide sequence within a cell. The m5C methylated polynucleotides (GIT) include an oligonucleotide imprinting element (IE) that has a first strand and a second strand complementary to the first strand. The first strand can include at least one m5CG sequence which is paired with an unmethylated CG sequence on the second strand. Alternatively, the first strand can include at least one m5CN1G sequence paired with an unmethylated CN2G sequence on said second strand, wherein N1 is any nucleotide, and N2 is a nucleotide that pairs with N1. The m5C methylated polynucleotides also include a single-stranded oligonucleotide guiding element (GE) that is complementary to a target nucleotide sequence. The guiding element includes at least one m5CG sequence m5CG or at least one 5CN3G sequence, wherein N3 is any nucleotide. The imprinting element and guiding element are operably linked such that the polynucleotide is capable of inducing methylation at the target nucleotide sequence. The oligonucleotide HepKex which targets the most proximal promoter of IGf2 can reach the nuclei of tested cell line and inhibit expression of IGf2 in animal and normal and cancer cell lines. The invention showed that oligonucleotide HepKex has anti-tumor activity in nude mice. The invention demonstrated that the GE fragment of a GIT significantly enhances the inhibition efficiency of the GIT.

IC ICM C12N
CC 3-4 (Biochemical Genetics)
IT **Drug delivery systems**
(liposomes, m5C methylated oligonucleotide encapsulated in; gene inactivation by targeted DNA methylation using a m5C methylated oligonucleotide containing an imprinting element and a guiding element)
IT **DNA**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(methylation; gene inactivation by targeted DNA methylation using a m5C methylated oligonucleotide containing an imprinting element and a guiding element)

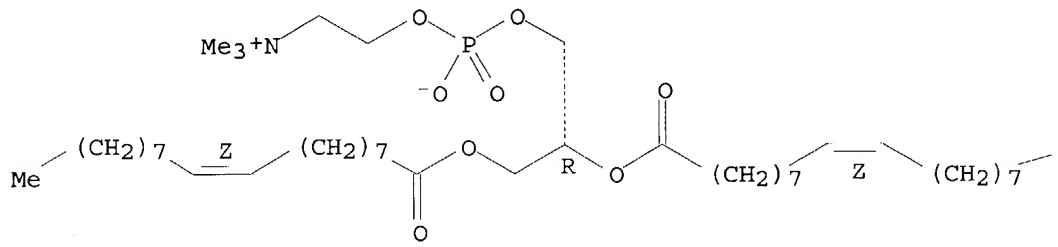
IT 2462-63-7, DOPE **4235-95-4**, DOPC **104162-48-3**, DOTMA
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(liposome encapsulating m5C methylated oligonucleotide made of; gene inactivation by targeted DNA methylation using a m5C methylated oligonucleotide containing an imprinting element and a guiding element)

IT **4235-95-4**, DOPC **104162-48-3**, DOTMA
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(liposome encapsulating m5C methylated oligonucleotide made of; gene inactivation by targeted DNA methylation using a m5C methylated oligonucleotide containing an imprinting element and a guiding element)

RN 4235-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A

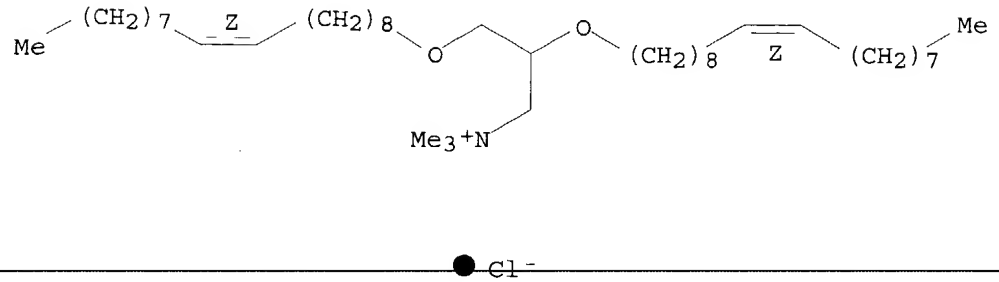


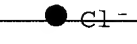
PAGE 1-B

Me

RN 104162-48-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.





L52 ANSWER 24 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:661307 HCAPLUS
DOCUMENT NUMBER: 135:231754
TITLE: Preparation of nanocapsules with polyelectrolyte envelope and liposome core
INVENTOR(S): Panzner, Steffen; Endert, Gerold; Essler, Frank; Behrens, Anja; Lutz, Silke; Panzner, Cornelia
PATENT ASSIGNEE(S): Novosom G.m.b.H., Germany
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064330	A1	20010907	WO 2001-EP2397	20010302
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10010264	A1	20010913	DE 2000-10010264	20000302
EP 1289642	A1	20030312	EP 2001-923626	20010302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003525258	T2	20030826	JP 2001-563221	20010302
US 2003157181	A1	20030821	US 2002-220590	20020903

PRIORITY APPLN. INFO.: DE 2000-10010264 A 20000302
WO 2001-EP2397 W 20010302

AB The invention concerns the nanoencapsulation of liposomes with layers of oppositely charged polyelectrolytes in order to increase the stability of liposomes. Microcapsules with a diameter of 20 nm to 40 μm are prepared The liposome template particles are provided in an aqueous medium, elec. recharged with a polyelectrolyte, recharged again with a second polyelectrolyte that is complementary to the first polyelectrolyte without intermediate separating or washing steps, and continuing, if required, this process with alternately charged polyelectrolytes. Crosslinking of the obtained structure using e.g. glutaraldehyde can be added. The method is used for the preparation of microcrystals, drug delivery systems, herbicides,

pesticides and pigments. Thus 20 mol% DPPC and 80 mol% DPPG were dissolved in isopropanol; the solvent was evaporated in vacuum. The lipid was rehydrated in buffer to result a 25 mM suspension, this was followed by freezing, thawing and filtration through a 200 nm polycarbonate membrane. The obtained liposomes were diluted with buffer to 0.2 mM; 1 mg/L and 5 mg/L solns. of albumin and heparin were prepared The polymer solns. were added to the liposomes one at a time; the procedure was repeated three times, thus resulting six layers. The product was treated with glutaraldehyde, dialyzed and concentrated The nanoparticles were stable in 150 mM sodium chloride; injected into Wistar rats; the rats survived at least for 24 h.

IC ICM B01J013-02
ICS B01J013-22

CC 63-8 (Pharmaceuticals)

IT **Drug delivery systems**
(liposomes; preparation of nanocapsules with polyelectrolyte envelope and liposome core)

IT **Drug delivery systems**
(microcapsules; preparation of nanocapsules with polyelectrolyte envelope and liposome core)

IT **Drug delivery systems**
(nanocapsules; preparation of nanocapsules with polyelectrolyte envelope and liposome core)

IT **Drug delivery systems**
(nanoparticles; preparation of nanocapsules with polyelectrolyte envelope and liposome core)

IT Agglutinins and Lectins
Amines, biological studies
Antibodies
Avidins
Carboxylic acids, biological studies
Ceramides
Collagens, biological studies
Enzymes, biological studies
Fibrinogens
Fibronectins
Hemoglobins
Myoglobins
Nucleic acids
Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphatidylglycerols
Phosphatidylinositols
Proteins, general, biological studies
Sphingolipids
Vitronectin
RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of nanocapsules with polyelectrolyte envelope and liposome core)

IT 57-09-0, Cetyltrimethyl ammonium bromide 59-02-9, α-Tocopherol 1256-86-6, Cholesterolsulfate 1510-21-0, Cholesterol hemisuccinate 2462-63-7 **2644-64-6** 4537-77-3 9000-01-5, Gum Arabic 9000-07-1, Carrageenan 9000-36-6, Karaya gum 9000-69-5, Pectin 9001-62-1, Lipase 9001-92-7, Protease 9002-98-6 9003-01-4, Polyacrylic acid 9003-05-8, Polyacrylamide 9003-39-8, Polyvinylpyrrolidone 9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9012-36-6, Agarose 9012-37-7, Acylase 9012-76-4, Chitosan 9013-19-8, Isomerase 9013-20-1, Streptavidin 9013-79-0,

Esterase 9013-93-8, Phospholipase 9013-95-0, Levan 9027-41-2, Hydrolase 9031-66-7, Aminotransferase 9031-96-3, Peptidase 9047-56-7, Mutase 9055-04-3, Lyase 9055-15-6, Oxidoreductase 11028-71-0, Concanavalin A 11138-66-2, Xanthan gum 22413-78-1, Inuline 25104-18-1, Poly-L-lysine 25249-06-3, Polygalacturonic acid 27072-45-3, FITC 29894-36-8, Polymannuronic acid 30551-89-4, Polyallylamine 50851-57-5, Polystyrene sulfonic acid **104162-48-3**, N-[1-[2,3 Dioleyl(oxy)propyl]-N,N,N-trimethylammonium chloride **132172-61-3**, N-[1-(2,3 Dioleoyl(oxy)propyl]-N,N,N-trimethylammoniumchloride 137056-72-5

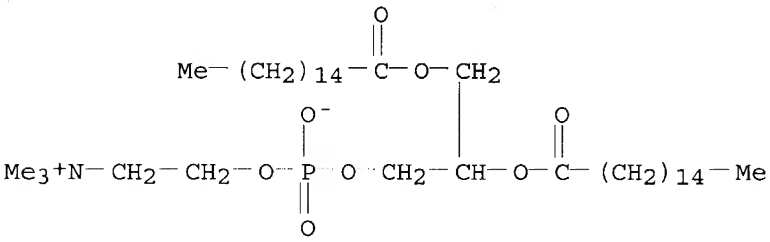
RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of nanocapsules with polyelectrolyte envelope and liposome core)

IT **2644-64-6 104162-48-3**, N-[1-[2,3 Dioleyl(oxy)propyl]-N,N,N-trimethylammonium chloride **132172-61-3**, N-[1-(2,3 Dioleoyl(oxy)propyl]-N,N,N-trimethylammoniumchloride

RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of nanocapsules with polyelectrolyte envelope and liposome core)

RN 2644-64-6 HCAPLUS

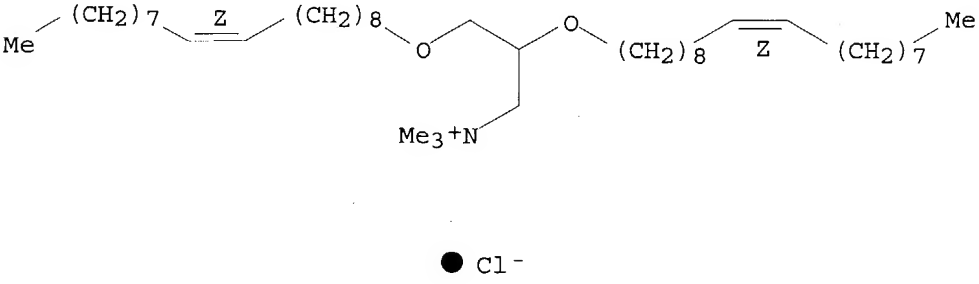
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 104162-48-3 HCAPLUS

CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



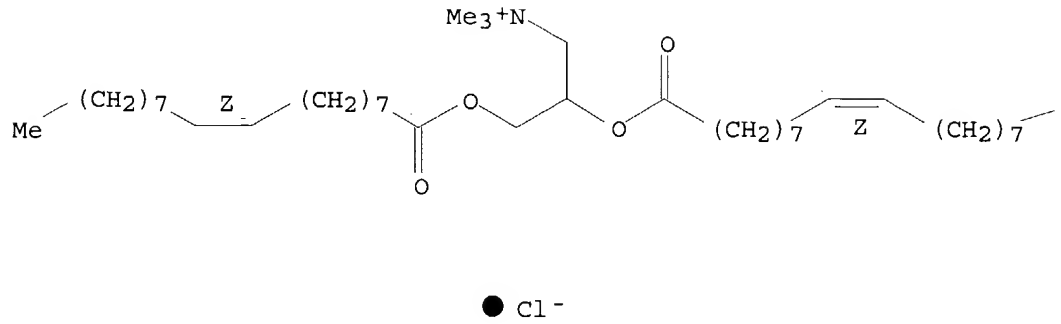
RN 132172-61-3 HCAPLUS

CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-,

chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 25 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:580638 HCAPLUS
DOCUMENT NUMBER: 136:236753
TITLE: On the mechanism whereby cationic lipids promote intracellular delivery of polynucleic acids
AUTHOR(S): Hafez, I. M.; Maurer, N.; Cullis, P. R.
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of British Columbia, Vancouver, BC, Can.
SOURCE: Gene Therapy (2001), 8(15), 1188-1196
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mechanism whereby cationic lipids destabilize cell membranes to facilitate the intracellular delivery of macromols. such as plasmid DNA or antisense oligonucleotides is not well understood. Here, the authors show that cationic lipids can destabilize lipid bilayers by promoting the formation of nonbilayer lipid structures. In particular, the authors show that mixts. of cationic lipids and anionic phospholipids preferentially adopt the inverted hexagonal (HII) phase. Further, the presence of "helper" lipids such as dioleoylphosphatidylethanolamine or cholesterol, lipids that enhance cationic lipid-mediated transfection of cells also facilitate the formation of the HII phase. It is suggested that the ability of cationic lipids to promote nonbilayer structures in combination with anionic phospholipids leads to disruption of the endosomal membrane

following uptake of nucleic acid-cationic lipid complexes into cells, thus facilitating cytoplasmic release of the plasmid or oligonucleotide.

CC 63-5 (Pharmaceuticals)

IT **Drug delivery systems**
(liposomes; mechanism whereby cationic lipids with anionic phospholipids promote intracellular delivery of polynucleic acids)

IT **DNA**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism whereby cationic lipids with anionic phospholipids promote intracellular delivery of polynucleic acids)

IT 107-64-2, Distearyldimethylammonium chloride 4004-05-1, DOPE **4235-95-4**, DOPC 7212-69-3, DODAC 40290-42-4, DPPS 61617-08-1 70614-14-1, DOPS **104162-48-3**, DOTMA 131692-03-0, OSDAC 137056-72-5, DC-Chol **144189-73-1**, DOTAP 185435-28-3, POPG 403479-92-5
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism whereby cationic lipids with anionic phospholipids promote intracellular delivery of polynucleic acids)

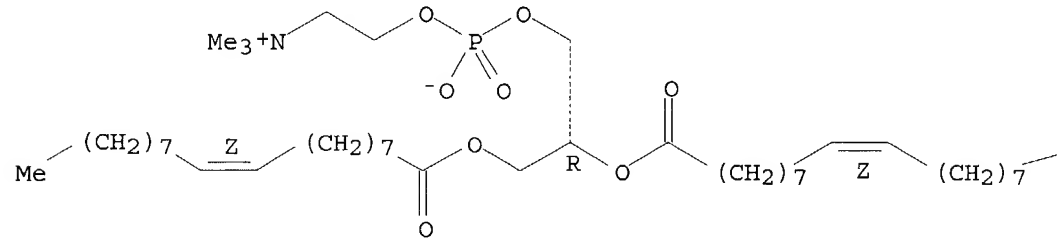
IT **4235-95-4**, DOPC **104162-48-3**, DOTMA **144189-73-1**, DOTAP
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism whereby cationic lipids with anionic phospholipids promote intracellular delivery of polynucleic acids)

RN 4235-95-4 HCAPLUS

CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



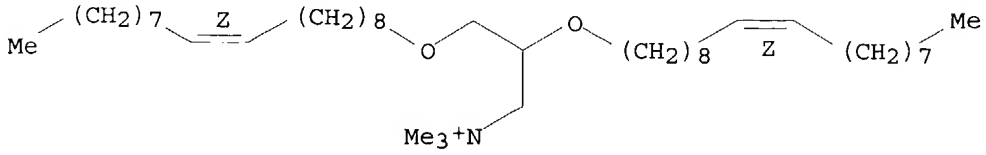
PAGE 1-B

Me

RN 104162-48-3 HCAPLUS

CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



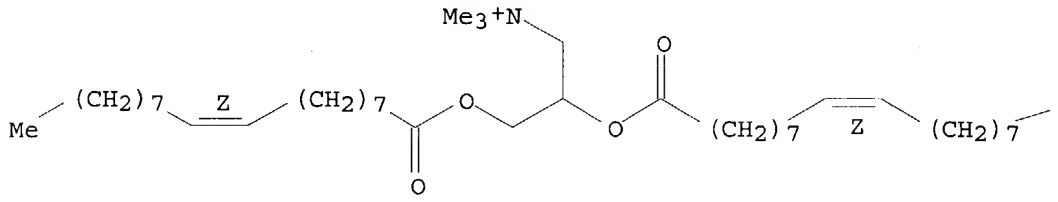
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

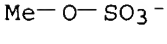
PAGE 1-A



PAGE 1-B

CM 2

CRN 21228-90-0
CMF C H3 O4 S



REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 26 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:575639 HCAPLUS
DOCUMENT NUMBER: 135:284583
TITLE: Structures of lipid-DNA complexes: supramolecular assembly and gene delivery
AUTHOR(S): Safinya, C. R.
CORPORATE SOURCE: Materials Department, Physics Department and Biomolecular Science and Engineering Program, University of California, Santa Barbara, CA, 93106, USA
SOURCE: Current Opinion in Structural Biology (2001), 11(4), 440-448
CODEN: COSBEF; ISSN: 0959-440X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with refs. Recently, there has been a flurry of exptl. work on understanding the supramol. assemblies that are formed when cationic liposomes (CLs) are mixed with DNA. From a biomedical point of view, CLs (vesicles) are empirically known to be carriers of genes (sections of DNA) in nonviral gene delivery applications. Although viral-based carriers of DNA are presently the most common method of gene delivery, nonviral synthetic methods are rapidly emerging as alternative carriers, because of their ease of production and non-immunogenicity (viral carriers very often evoke an undesirable and potentially lethal immune response). At the moment, cationic-lipid-based carriers have emerged as the most popular nonviral method to deliver genes in therapeutic applications, for example, CL carriers are used extensively in clin. trials worldwide. However, because the mechanism of transfection (the transfer of DNA into cells by CL carriers, followed by expression) of CL-DNA complexes remains largely unknown, the measured efficiencies are, at present, very low. The low transfection efficiencies of current nonviral gene delivery methods are the result of poorly understood transfection-related mechanisms at the mol. and self-assembled levels. Recently, work has been carried out on determining the supramol. structures of CL-DNA complexes by the quant. technique of synchrotron X-ray diffraction. When DNA is mixed with CLs (composed of mixts. of cationic DOTAP and neutral DOPC lipids), the resulting CL-DNA complex consists of a multilamellar structure (LαC) comprising DNA monolayers sandwiched between lipid bilayers. The existence of a different columnar inverted hexagonal (HIIC) phase in CL-DNA complexes was also demonstrated using synchrotron X-ray diffraction. Ongoing functional studies and optical imaging of cells are expected to clarify the relationship between the supramol. structures of CL-DNA complexes and transfection efficiency.

CC 6-0 (General Biochemistry)
Section cross-reference(s): 3

IT **DNA**
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(complexes, with cationic liposomes; supramol. assembly and structure of, and gene delivery by, lipid-DNA complexes)

IT **Drug delivery systems**
(liposomes, cationic, complexes with DNA; supramol. assembly and structure of, and gene delivery by, lipid-DNA complexes)

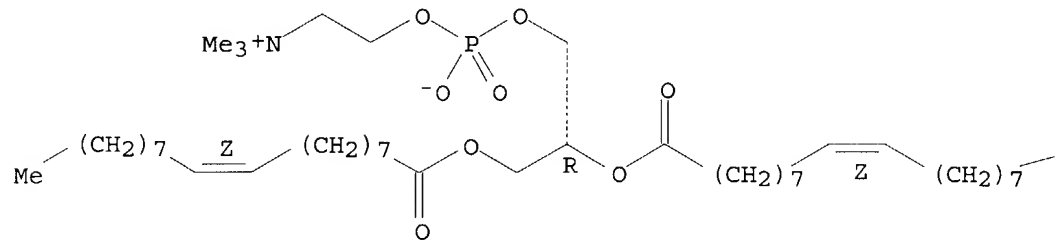
IT **4235-95-4D**, DOPC, liposomes containing, complexes with DNA
144189-73-1D, DOTAP, liposomes containing, complexes with DNA
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(supramol. assembly and structure of, and gene delivery by, lipid-DNA complexes)

IT **4235-95-4D**, DOPC, liposomes containing, complexes with DNA
144189-73-1D, DOTAP, liposomes containing, complexes with DNA
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(supramol. assembly and structure of, and gene delivery by, lipid-DNA complexes)

RN 4235-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

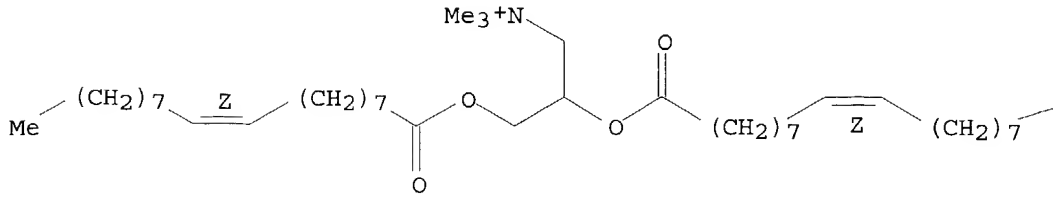
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me— O— SO_3^-

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 27 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:448754 HCAPLUS
DOCUMENT NUMBER: 136:145873
TITLE: Interplay in lipoplexes between type of pDNA promoter and lipid composition determines transfection efficiency of human growth hormone in NIH3T3 cells in culture
AUTHOR(S): Kerner, M.; Meyuhas, O.; Hirsch-Lerner, D.; Rosen, L. J.; Min, Z.; Barenholz, Y.
CORPORATE SOURCE: Department of Biochemistry, Hebrew University-Hadassah Medical School, Jerusalem, 91120, Israel
SOURCE: Biochimica et Biophysica Acta (2001), 1532(1-2), 128-136
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study was aimed to investigate if and to what extent there is an interplay between lipoplex physicochem. properties and plasmid promoter type affecting transfection efficiency in vitro. To reduce the number of variables only one cell type (NIH3T3 cells), one gene (human growth hormone), one cationic lipid (DOTAP) in a plasmid >85% in supercoiled form, and the same medium conditions were used. The variables of the

physicochem. properties included presence and type of helper lipid (DOPE, DOPC, or cholesterol, all in 1:1 mol ratio with DOTAP), size and lamellarity of the liposomes used for lipoplex preparation (large unilamellar vesicles, LUV, vs. multilamellar vesicles, MLV), and DNA-/cationic lipid+ charge ratio, all containing the same human growth hormone but differing in their promoter enhancer region. Two of the promoters were of viral origin: (a) SV40 promoter (simian virus early promoter) and (b) CMV promoter (cytomegalovirus early promoter); two were of mammalian cell origin: (c) PABP promoter (human poly(A)-binding protein promoter) and (d) S16 promoter (mouse ribosomal protein (rp) S16 promoter). Transfection studies showed that, irresp. of promoter type, large (≥500 nm) MLV were superior to .apprx.100 nm LUV; the extent of superiority was dependent on liposome lipid composition (larger for 100% DOTAP and DOTAP/DOPE than for DOTAP/DOPC and DOTAP/cholesterol). The optimal DNA-/DOTAP+ charge ratio for all types of lipoplexes used was 0.2 or 0.5 (namely, when the lipoplexes were pos. charged). Scoring the six best lipoplex formulations (out of 128 studied) revealed the following order: pCMV (DOTAP/DOPE)»pSV (DOTAP/DOPE)=pCMV(DOTAP/cholesterol)=pS16 (100% DOTAP)=pS16 DOTAP/DOPE»pCMV (DOTAP/DOPC). The lack of trivial consistency in the transfection efficiency score, the pattern of transfection efficiency, and statistical anal. of the data suggest that there is cross-talk between promoter type and lipoplex lipid composition, which may be related to the way the promoter is associated with the lipids.

CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 1, 14

IT **DNA**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(complexes, with lipids; interplay in lipoplexes between type of pDNA promoter and lipid composition dets. transfection efficiency of human growth hormone in NIH3T3 cells in culture)

IT **Drug delivery systems**
(liposomes; interplay in lipoplexes between type of pDNA promoter and lipid composition dets. transfection efficiency of human growth hormone in NIH3T3 cells in culture)

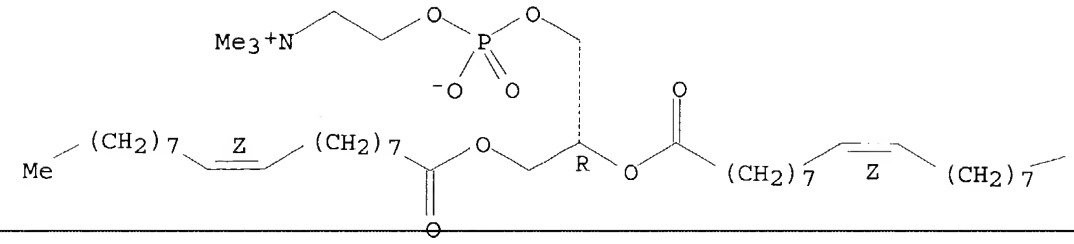
IT 2462-63-7, DOPE **4235-95-4**, DOPC **144189-73-1**, DOTAP
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(interplay in lipoplexes between type of pDNA promoter and lipid composition dets. transfection efficiency of human growth hormone in NIH3T3 cells in culture)

IT **4235-95-4**, DOPC **144189-73-1**, DOTAP
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(interplay in lipoplexes between type of pDNA promoter and lipid composition dets. transfection efficiency of human growth hormone in NIH3T3 cells in culture)

RN 4235-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

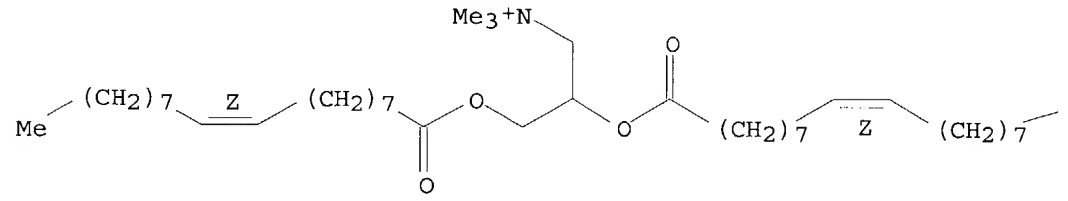
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A

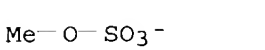


PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 28 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:382812 HCAPLUS
DOCUMENT NUMBER: 136:68329
TITLE: Membrane fusion induced by a lipopeptidic epitope from VP3 capsid protein of hepatitis A virus
AUTHOR(S): Chavez, Abelardo; Pujol, Montserrat; Alsina, M. Asuncion; Cajal, Yolanda
CORPORATE SOURCE: Department of Physical Chemistry, School of Pharmacy, University of Barcelona, Barcelona, 08028, Spain
SOURCE: Luminescence (2001), 16(2), 135-143
CODEN: LUMIFC; ISSN: 1522-7235
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Palmitoyl-VP3(110-121) (PVP3) is a synthetic lipopeptide derivative of a continuous epitope from the VP3 capsid protein of hepatitis A virus, and it is highly immunogenic in vivo. We have investigated the interaction of PVP3 with lipid model membranes of varying surface charge. Binding of PVP3 to anionic vesicles of PC/SM/PE/PS; (PC) 1-palmitoyl-2-oleoylphosphatidylcholine, (SM) sphingomyelin, (PE) 1,2-dipalmitoyl-phosphatidylethanolamine and (PS) L-α-phosphatidyl-L-serine, a composition that mimics the lipid component of natural membranes, was determined by tryptophan fluorescence and quenching expts. In addition, and given the anionic net charge of the lipopeptide, binding to zwitterionic (PC/SM/PE) and cationic PC/SM/PE/DOTAP (DOTAP) 1,2-dioleoyl-3-trimethylammonium-propane mixts. was also determined PVP3 binds to all three types of vesicles, but it adopts different forms depending on the elec. charge of the interface. This conclusion is supported by the insertion of PVP3 into lipid monolayers of the same charges spread at the air-water interface. The bound lipopeptide has membrane-destabilizing effects in all three vesicle compns., as demonstrated by leakage of vesicle contents, whereas lipid mixing only occurs in cationic liposomes. Our results provide useful information for the design of a liposomal system that promotes a direct delivery of the membrane-incorporated immunogen to the immunocompetent cells, potentially increasing the immune response from the host.

CC 15-2 (Immunochemistry)
Section cross-reference(s): 63

IT **Drug delivery systems**
(liposomes; membrane fusion induced by a lipopeptidic epitope from VP3 capsid protein of hepatitis A virus)

IT **Epitopes**
Hepatitis A virus
(membrane fusion induced by a lipopeptidic epitope from VP3 capsid protein of hepatitis A virus)

IT **Antigens**

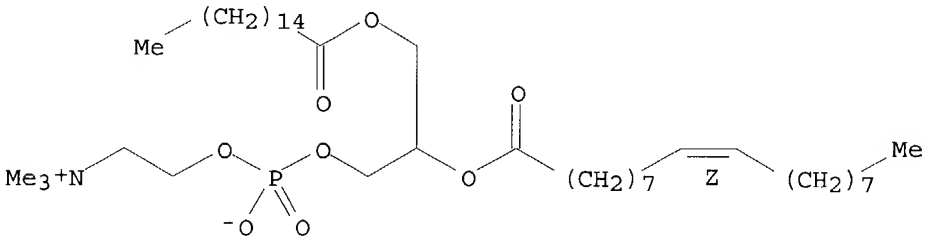
Phosphatidylserines
Sphingomyelins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(membrane fusion induced by a lipopeptidic epitope from VP3 capsid protein of hepatitis A virus)

IT 5681-36-7, 1,2-Dipalmitoyl-phosphatidylethanolamine **26662-91-9**, 1-Palmitoyl-2-oleoylphosphatidylcholine **144189-73-1**, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(membrane fusion induced by a lipopeptidic epitope from VP3 capsid protein of hepatitis A virus)

IT **26662-91-9**, 1-Palmitoyl-2-oleoylphosphatidylcholine **144189-73-1**, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(membrane fusion induced by a lipopeptidic epitope from VP3 capsid protein of hepatitis A virus)

RN 26662-91-9 HCAPLUS
CN 3,5,8-Trioxa-4-phosphahexacos-17-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-9-oxo-7-[[(1-oxohexadecyl)oxy]methyl]-, inner salt, 4-oxide, (17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



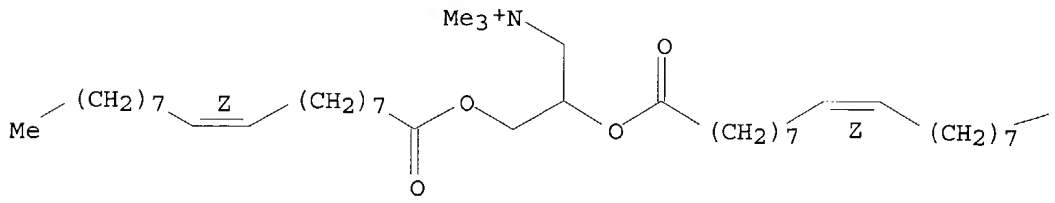
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

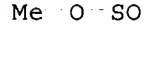
Double bond geometry as shown.

PAGE 1-A



CM 2

CRN 21228-90-0
CMF C H3 O4 S



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

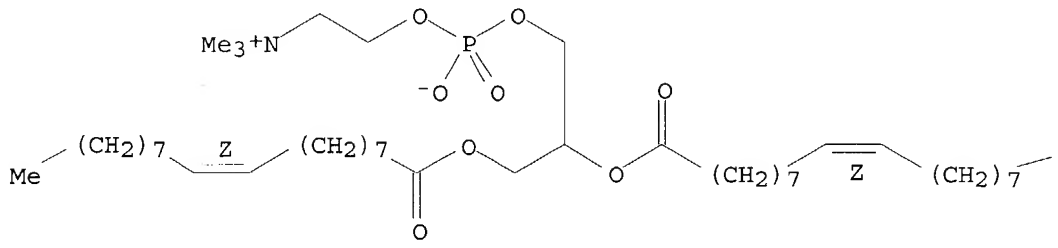
L52 ANSWER 29 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:330326 HCAPLUS
DOCUMENT NUMBER: 135:170593
TITLE: Efficient gene delivery using anionic liposome-complexed polyplexes (LPDII)
AUTHOR(S): Guo, Wenjin; Lee, Robert J.
CORPORATE SOURCE: Division of Pharmaceutics and Pharmaceutical Chemistry, College of Pharmacy, The Ohio State University, Columbus, OH, 43210, USA
SOURCE: Bioscience Reports (2000), 20(5), 419-432
CODEN: BRPTDT; ISSN: 0144-8463
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Synthetic gene transfer vectors based on polyplexes complexed to anionic liposomes (LPDII vectors) were characterized for their transfection efficiency in cultured mammalian cells. The effects of polycation to DNA ratio, lipid to DNA ratio, choice of polycation and lipid composition were systematically evaluated in human oral carcinoma KB cells, using a luciferase reporter gene. For LPDII formulations containing poly(L-lysine) and dioleoylphosphatidylethanolamine/cholesteryl hemisuccinate (DOPE/CHEMS) anionic liposomes, at a constant lipid to DNA ratio, an increase in the polycation/DNA (N/P) ratio resulted in an increase in transfection activity. Meanwhile, the optimal lipid to DNA ratio for efficient gene delivery was influenced by the N/P ratio used, and was increased at higher N/P ratios. For the DNA condensing agent, poly(L-lysine) could be replaced by polyethylenimine (PEI) as the DNA condensing agent in the formulations. For the lipidic components, CHEMS could be replaced by other anionic lipids including oleic acid, dicetylphosphate and phosphatidylserine, but DOPE, a fusogenic helper lipid, could not be replaced by dioleolyphosphatidylcholine. LPDII formulation showed significantly less cytotoxicity compared to the commonly used cationic liposomes or PEI mediated transfection and several cell lines were transfected with high efficiency. LPDII vectors avoid the use of toxic cationic lipids and may have potential application in gene therapy.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 3
IT **DNA**
Phosphatidylserines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficient gene delivery using anionic liposome-complexed polyplexes)
IT **Drug delivery systems**
(liposomes; efficient gene delivery using anionic liposome-complexed polyplexes)
IT 112-80-1, Oleic acid, biological studies 1510-21-0, Cholesteryl hemisuccinate 2197-63-9, Dicetylphosphate 2462-63-7, Dioleoylphosphatidylethanolamine 3700-67-2, Dimethyldioctadecylammonium bromide 6811-55-8, Dioleoylphosphatidylserine 9002-98-6, Polyethylenimine 25104-18-1, Poly(L-lysine) 38000-06-5, Poly(L-lysine) **68737-67-7**, Dioleoylphosphatidylcholine **144189-73-1**, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficient gene delivery using anionic liposome-complexed polyplexes)
IT **68737-67-7**, Dioleoylphosphatidylcholine **144189-73-1**, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficient gene delivery using anionic liposome-complexed polyplexes)
RN 68737-67-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (18Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

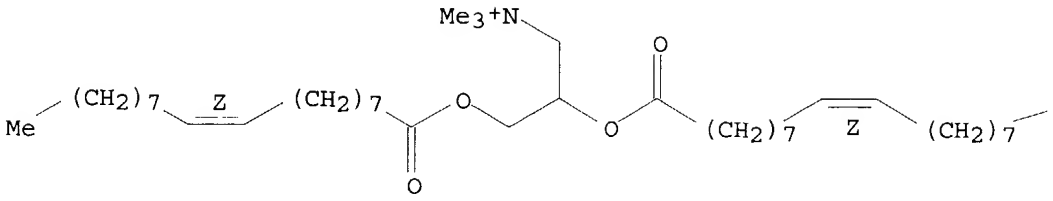
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO_3^-

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 30 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:275412 HCAPLUS
DOCUMENT NUMBER: 136:189179
TITLE: Liposome-mediated DNA **vaccination**: the effect of vesicle composition
AUTHOR(S): Perrie, Y.; Frederik, P. M.; Gregoriadis, G.
CORPORATE SOURCE: Centre for Drug Delivery Research, School of Pharmacy, 29-39 Brunswick Square, University of London, London, WC1N 1AX, UK
SOURCE: Vaccine (2001), 19(23-24), 3301-3310
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Liposome-entrapped DNA has been shown to enhance the potency of DNA **vaccines**, possibly by facilitating uptake of the plasmid by antigen-presenting cells (APC). In this paper, we have investigated the influence of the liposomal composition and surface charge on such potency.

Plasmid DNA pRc/CMV HBS encoding the S (small) region of hepatitis B surface antigen was entrapped within cationic liposomes of various compns. and surface charges with high efficiency (88-97% of the amount used) by the dehydration-rehydration method that generates dehydration-rehydration vesicles (DRV). Cryo-electron microscopy revealed that DNA-containing DRV (DRV(DNA)) were multilamellar. In **immunization** studies, female Balb/c mice were given two to four i.m. injections of 10 μg naked or liposome-entrapped pRc/CMV HBS and bled at time intervals. Results indicate that the lipid composition of the DRV(DNA) influences the strength of the humoral response (Ig (Ig)G subclasses) with inclusion of dioleoyl phosphatidylethanolamine (DOPE) or phosphatidylethanolamine (PE) in the liposomal structure contributing to greater responses. DRV(DNA) in which the DOPE or PE were omitted or substituted with cholesterol led to significant reduction of humoral responses against the encoded antigen. Replacing phosphatidylcholine (PC) in the DRV(DNA) with the high-melting distearoyl phosphatidylcholine also contributed to lower responses. In other expts., IgG responses were monitored in mice **immunized** with pRc/CMV HBS entrapped in DRV composed of PC and DOPE as before but incorporating increasing amts. of DOTAP (1-16 μmol). Maximal IgG responses were observed at 10 wk after the first of four injections and suggested a trend of higher responses when 4 or 8 μmol DOTAP was present in the DRV(DNA) formulation. Cell-mediated **immunity** (measured in terms of endogenous antigen-specific splenic interferon-γ) in mice **immunized** with pRc/CMV HBS entrapped in liposomes composed of PC, DOPE and DOTAP (16:8:4 molar ratio) was much greater than in animals treated with naked plasmid. These results indicate that liposome-mediated DNA **immunization** is more effective than the use of naked DNA, and also suggest that the presence of fusogenic phosphatidylethanolamine in DRV in conjunction with a low-melting phosphatidylcholine and an appropriate content of cationic lipid might contribute to more effective liposomal DNA **vaccines.** The notion that liposomes improve immune responses to the plasmid-encoded **vaccine** by facilitating the latter's uptake by APC was supported by the observation that in Balb/c mice injected i.m. with liposome-entrapped pCMV. Enhanced green fluorescent protein, expression of the gene in terms of fluorescence intensity in the draining lymph nodes, was much greater than in animals treated with the naked plasmid.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 15

ST DNA **vaccine** liposome compn surface charge

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hepatitis B surface; vesicle composition effect on liposome-mediated DNA **vaccination**)

IT **Vaccines**
(hepatitis B; vesicle composition effect on liposome-mediated DNA **vaccination**)

IT **Drug delivery systems**
(liposomes, multilamellar; vesicle composition effect on liposome-mediated DNA **vaccination**)

IT Zeta potential
(vesicle composition and surface charge effect on liposome-mediated DNA **vaccination**)

IT Particle size
Plasmid vectors
Vaccines
(vesicle composition effect on liposome-mediated DNA **vaccination**)

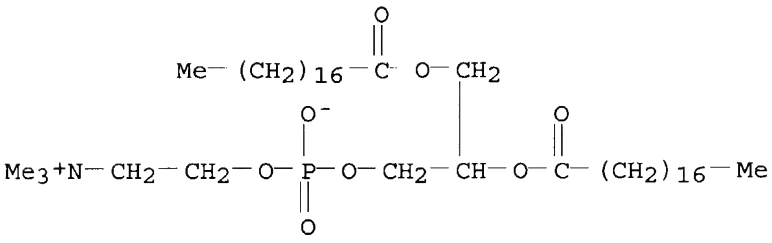
IT **DNA**
Phosphatidylcholines, biological studies

Phosphatidylethanolamines, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vesicle composition effect on liposome-mediated DNA **vaccination**)

IT 57-88-5, Cholesterol, biological studies 2462-63-7, Dioleoyl phosphatidylethanolamine **4539-70-2**, Distearoyl phosphatidylcholine **144189-73-1**, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vesicle composition effect on liposome-mediated DNA **vaccination**)

IT **4539-70-2**, Distearoyl phosphatidylcholine **144189-73-1**, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vesicle composition effect on liposome-mediated DNA **vaccination**)

RN 4539-70-2 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



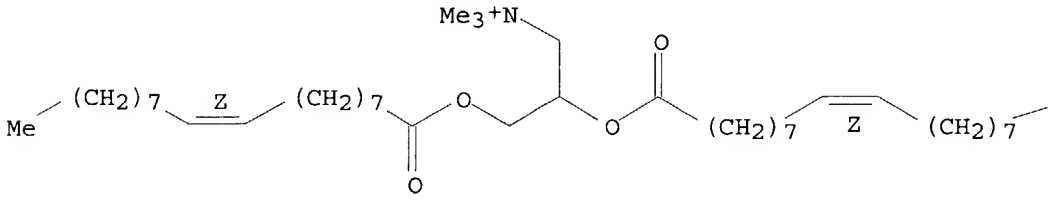
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO_3^-

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 31 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:265230 HCAPLUS
DOCUMENT NUMBER: 134:285563
TITLE: Liposome-entrapped DNA oral **vaccines**
INVENTOR(S): Gregoriadis, Gregory; Perrie, Yvonne
PATENT ASSIGNEE(S): Lipoxen Limited, UK
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001024773	A1	20010412	WO 2000-GB3773	20001002
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1217989	A1	20020703	EP 2000-964471	20001002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003529550	T2	20031007	JP 2001-527772	20001002

PRIORITY APPLN. INFO.: EP 1999-307786 A 19991001
WO 2000-GB3773 W 20001002
OTHER SOURCE(S): MARPAT 134:285563

AB An oral **vaccine** comprises liposomes and complexed or, preferably, entrapped DNA operatively encoding an antigen, in which the liposomes are formed from components including cationic compds. and zwitterionic phospholipids. The hydrophobic groups within the liposome forming compds. must include at least one group which is saturated This is believed to raise the transition temperature, rendering the liposomes more stable when delivered orally. The compns. have been found to give detectable increased in IgA levels, secreted Igs of importance in efficacious oral **vaccine** delivery. Liposomes comprising phosphatidylcholine 32, dioleoyl phosphatidylethanolamine 16, and dioleoyl trimethylammonium propane 8 μmoles were prepared using the dehydration-rehydration method. PRc/CMV HBS plasmid DNA encoding for the

small region of hepatitis B surface antigen was entrapped in the above liposome formulations. Entrapment complexation efficiency was 85-95%. **Immunization** of mice with the liposomes is described.

IC ICM A61K009-127
ICS A61K048-00; C12N015-88

CC 63-3 (Pharmaceuticals)

ST liposome phospholipid DNA oral **vaccine**

IT Lipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycerolipids; liposome-entrapped DNA oral **vaccines**)

IT Freeze drying
(liposome-entrapped DNA oral **vaccines**)

IT **Antigens**
DNA
Nucleic acids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-entrapped DNA oral **vaccines**)

IT Phosphatidylcholines, biological studies
Polynucleotides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-entrapped DNA oral **vaccines**)

IT **Drug delivery systems**
(liposomes; liposome-entrapped DNA **oral vaccines**)

IT **Vaccines**
(oral; liposome-entrapped DNA oral **vaccines**)

IT Drying
(spray; liposome-entrapped DNA oral **vaccines**)

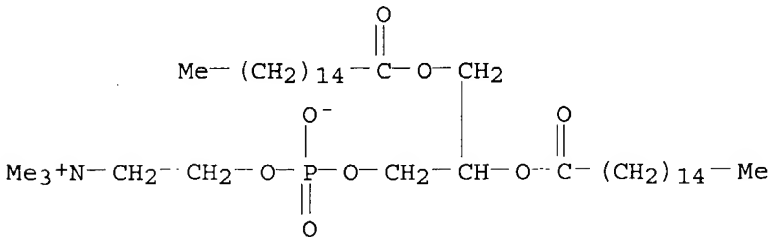
IT Phospholipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zwitterionic; liposome-entrapped DNA oral **vaccines**)

IT 57-88-5, Cholesterol, biological studies 2462-63-7, Dioleoyl phosphatidylethanolamine **2644-64-6**, Dipalmitoylphosphatidylcholine 4537-76-2, Distearoylphosphatidylethanolamine **4539-70-2**, Distearoylphosphatidylcholine 5681-36-7, Dipalmitoylphosphatidylethanolamine **113669-21-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-entrapped DNA oral **vaccines**)

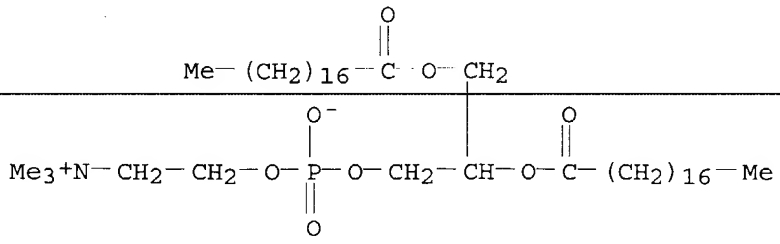
IT **2644-64-6**, Dipalmitoylphosphatidylcholine **4539-70-2**, Distearoylphosphatidylcholine **113669-21-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-entrapped DNA oral **vaccines**)

RN 2644-64-6 HCAPLUS

CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



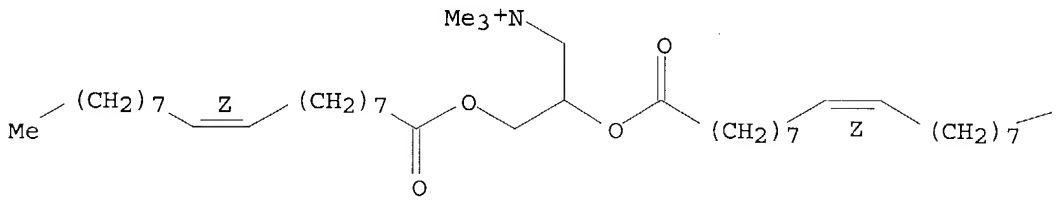
RN 4539-70-2 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 113669-21-9 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 32 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:241683 HCAPLUS
DOCUMENT NUMBER: 134:271256
TITLE: Methods of forming protein-linked lipidic microparticles, and compositions thereof
INVENTOR(S): Papahadjopoulos, Demetrios; Hong, Keelung; Zheng, Weiwen; Kirpotin, Dmitri B.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S., 26 pp., Cont.-in-part of U.S. Ser. No. 967,791.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6210707	B1	20010403	US 1998-76618	19980512
US 6071533	A	20000606	US 1997-967791	19971110
CA 2330741	AA	19991118	CA 1999-2330741	19990511
WO 9958694	A1	19991118	WO 1999-US10375	19990511
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9939834	A1	19991129	AU 1999-39834	19990511
AU 770111	B2	20040212		
EP 1078079	A1	20010228	EP 1999-922950	19990511
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002514432	T2	20020521	JP 2000-548485	19990511
US 6410049	B1	20020625	US 1999-420908	19991020
US 2002001612	A1	20020103	US 2001-765107	20010116
US 6528087	B2	20030304		
US 2002182249	A1	20021205	US 2002-121962	20020412
US 2003003143	A1	20030102	US 2002-177939	20020621

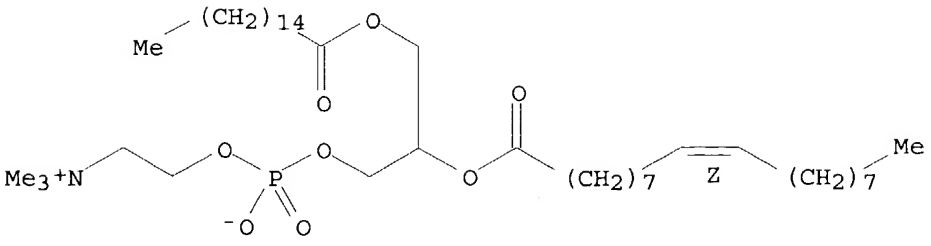
PRIORITY APPLN. INFO.:	US 1996-30578P	P	19961112
	US 1997-967791	A2	19971110
	US 1998-76618	A	19980512
	WO 1999-US10375	W	19990511
	US 1999-420908	A1	19991020
	US 2001-765107	A1	20010116

AB The present invention provides for lipid/nucleic acid complexes that have increased shelf life and high transfection activity in vivo following i.v. injection, and methods of preparing such complexes. The methods generally involve contacting a nucleic acid with an organic polycation to produce a condensed nucleic acid, and then combining the condensed nucleic acid with a lipid comprising an amphiphilic cationic lipid to produce the lipid/nucleic acid complex. This complex can be further stabilized by the addition of a hydrophilic polymer attached to hydrophobic side chains. The complex can also be made specific for specific cells, by incorporating a targeting moiety such as an Fab' fragment attached to a hydrophilic polymer. The present invention further relates to lipidic microparticles with attached proteins which have been first conjugated to linker mols. having a hydrophilic polymer domain and a hydrophobic domain capable of stable association with the microparticle, or proteins which have been engineered to contain a hydrophilic domain and a lipid moiety permitting stable association with the microparticle. For example, maleimido-propionylantido-PEG-distearoylphosphatidylethanolamine (Mal-PEG-DSPE) was prepared, conjugated with a single chain Fv antibody reactive against HER2 oncoprotein, and formulated into immunoliposomes for targeting of HER2-overexpressing human breast cancer cells.

IC ICM A61K009-127
NCL 424450000

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 3
IT **Drug delivery systems**
(immunoliposomes; preparation of protein-linked lipidic microparticles for targeting of nucleic acids)
IT **Drug delivery systems**
(injections, i.v.; preparation of protein-linked lipidic microparticles for targeting of nucleic acids)
IT **Drug delivery systems**
(liposomes; preparation of protein-linked lipidic microparticles for targeting of nucleic acids)
IT **Drug delivery systems**
(microemulsions; preparation of protein-linked lipidic microparticles for targeting of nucleic acids)
IT **Drug delivery systems**
(microparticles; preparation of protein-linked lipidic microparticles for targeting of nucleic acids)
IT Chromatography
Dialysis
Drug targeting
Gene therapy
Protein sequences
Salting-out
Transformation, genetic
(preparation of protein-linked lipidic microparticles for targeting of nucleic acids)
IT **DNA**
Enzymes, biological studies
Growth factors, animal
Hormones, animal, biological studies
Lipids, biological studies
Nucleic acids
Polymers, biological studies
Proteins, general, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of protein-linked lipidic microparticles for targeting of nucleic acids)
IT 57-88-5, Cholesterol, biological studies 2462-63-7, DOPE 2591-17-5, D-Luciferin 3700-67-2, Dimethyldioctadecylammonium bromide **26662-91-9**, 1-Palmitoyl-2-oleoyl-phosphatidylcholine 124050-77-7, DOGS 127512-29-2, DODAP 137056-72-5, DC-chol **144189-73-1**, DOTAP 178744-28-0 216165-62-7 321975-96-6 331942-29-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of protein-linked lipidic microparticles for targeting of nucleic acids)
IT **26662-91-9**, 1-Palmitoyl-2-oleoyl-phosphatidylcholine
144189-73-1, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of protein-linked lipidic microparticles for targeting of nucleic acids)
RN 26662-91-9 HCAPLUS
CN 3,5,8-Trioxa-4-phosphahexacos-17-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-9-oxo-7-[[(1-oxohexadecyl)oxy]methyl]-, inner salt, 4-oxide, (17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



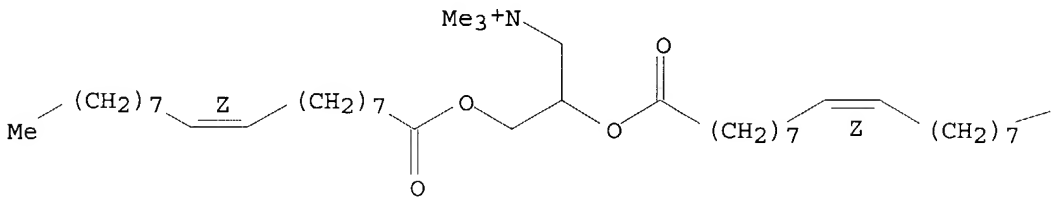
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

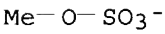
PAGE 1-A



PAGE 1-B

CM 2

CRN 21228-90-0
CMF C H3 O4 S



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 33 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:185553 HCAPLUS
DOCUMENT NUMBER: 134:227389
TITLE: Cationic liposome delivery of taxanes to angiogenic blood vessels
INVENTOR(S): McDonald, Donald M.; McLean, John W.; Thurston, O. Gavin
PATENT ASSIGNEE(S): Regents of the University of California, USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001017508	A1	20010315	WO 2000-US24579	20000908
WO 2001017508	C2	20021003		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000013866	A	20020514	BR 2000-13866	20000908
EP 1210065	A1	20020605	EP 2000-960004	20000908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
EE 200200127	A	20030415	EE 2002-127	20000908
JP 2003514768	T2	20030422	JP 2001-521299	20000908
ZA 2002001555	A	20030225	ZA 2002-1555	20020225
US 2002168355	A1	20021114	US 2002-161194	20020528

PRIORITY APPLN. INFO.:
US 1999-392976 A 19990909
US 1997-820337 A1 19970312
US 1998-127177 A2 19980731
WO 2000-US24579 W 20000908

AB Angiogenic endothelial cells are selectively targeted with lipid/DNA complexes or cationic liposomes containing a substance which affects the targeted cells by inhibiting or promoting their growth. A site of angiogenesis can be precisely located by administering cationic liposomes containing a detectable label. The complexes may comprise nucleotide constructs which are comprised of promoters which are selectively and exclusively activated in the environment of an angiogenic endothelial cell. For example, a formulation of small unilamellar liposomes composed of DOTAP/egg phosphatidylcholine/rhodamine DHPE/paclitaxel (50:47:1:2) was injected into mice infected with Mycoplasma pulmonis i.v. in a volume of 150 μL and 20 min later mice were injected with fluorescein-labeled Lycopersicon esculentum lectin to stain endothelial cells throughout the body. Paclitaxel-containing liposomes were taken up avidly by endothelial cells of airway blood vessels in trachea of infected mice while little uptake in blood vessels of the trachea of uninfected mice was observed

IC ICM A61K009-127
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT Angiogenesis

Angiogenesis inhibitors
Anti-inflammatory agents
Antitumor agents
Circulation
Drug targeting
Fluorescent indicators
Respiratory tract
(cationic liposome delivery of taxanes to angiogenic blood vessels)

IT **DNA**
Nucleotides, biological studies
Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Taxanes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic liposome delivery of taxanes to angiogenic blood vessels)

IT **Drug delivery systems**
(injections; cationic liposome delivery of taxanes to angiogenic blood vessels)

IT **Drug delivery systems**
(liposomes; cationic liposome delivery of taxanes to angiogenic blood vessels)

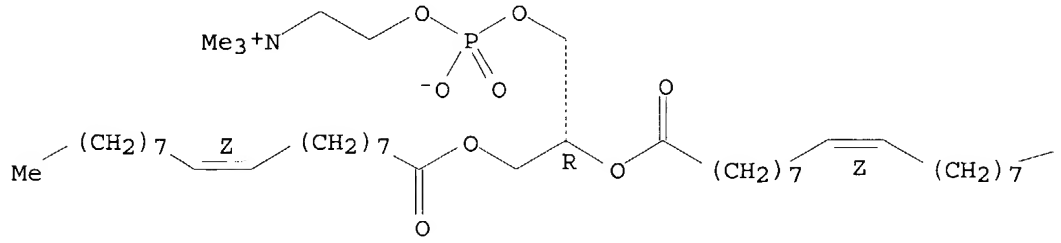
IT 57-88-5, Cholesterol, biological studies 2462-63-7, DOPE 3700-67-2, Dimethyldioctadecyl ammonium bromide **4235-95-4**, DOPC **144189-73-1**, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic liposome delivery of taxanes to angiogenic blood vessels)

IT **4235-95-4**, DOPC **144189-73-1**, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic liposome delivery of taxanes to angiogenic blood vessels)

RN 4235-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

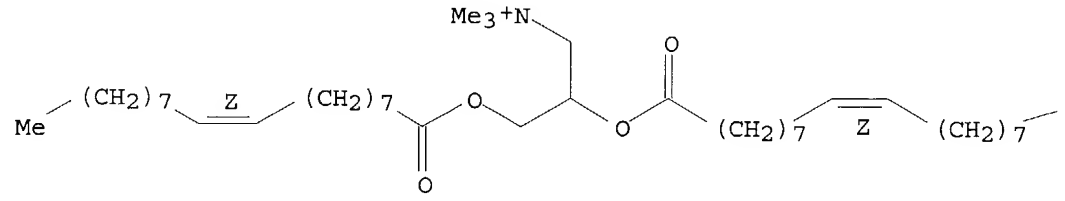
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO_3^-

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 34 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:755211 HCAPLUS
DOCUMENT NUMBER: 133:340208
TITLE: Novel compositions useful for delivering anti-inflammatory agents into a cell
INVENTOR(S): Unger, Evan C.; McCreery, Thomas; Sadewasser, David A.
PATENT ASSIGNEE(S): ImaRx Pharmaceutical Corp., USA
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1046394	A2	20001025	EP 2000-303249	20000418
EP 1046394	A3	20011010		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1999-294623 A 19990419

AB The present invention is directed, inter alia, to compns. and their use for delivering compds. into a cell. In a preferred embodiment, the compns. comprise, in combination with the compound to be delivered, an organic halide, a targeting ligand, and a nuclear localization sequence, optionally in the presence of a carrier. Ultrasound may be applied, if desired. The compns. are particularly suitable for the treatment of inflammatory diseases.

IC ICM A61K009-127
ICS A61K048-00; C12N015-88

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 34

IT Anti-inflammatory agents
Cations
Drug targeting
Gene therapy
Genetic vectors
Protein sequences
(peptide compns. useful for delivering anti-inflammatory agents into a cell)

IT **Antisense oligonucleotides**
Ribozymes
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(peptide compns. useful for delivering anti-inflammatory agents into a cell)

IT **Drug delivery systems**
(targeted; peptide compns. useful for delivering anti-inflammatory agents into a cell)

IT 57-09-0, Ctab 57-88-5, Cholesterol, biological studies 57-88-5D, Cholesterol, esters 124-30-1, Stearylamine 926-63-6, Dimethylammonium propane 1398-61-4, Chitin 2462-63-7, Dope 3282-73-3, Ddab 3614-36-6, Diacetyl phosphate **4235-95-4**, Dopc 4458-31-5, Diethylammonium propane 6561-76-8, Dcpe 9000-07-1, Carrageenan 9000-69-5, Pectin 9002-88-4D, Polyethylene, derivs. 9003-07-0D, Polypropylene, derivs. 9003-39-8, Polyvinylpyrrolidone 9004-32-4, Carboxymethylcellulose 9004-34-6, Cellulose, biological studies 9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid 9004-65-3, Hydroxypropyl methylcellulose 9005-32-7, Alginic acid 9005-79-2, Glycogen, biological studies 9005-82-7, Amylose 9007-27-6, Chondroitin 9012-36-6, Agarose 9012-72-0D, Glucan, derivs. 9013-95-0D, Levan, derivs. 9014-63-5D, Xylan, derivs. 9037-22-3, Amylopectin 9037-55-2D, Galactan, derivs. 9037-90-5D, Fructan, derivs. 9046-38-2D, Galacturonan, derivs. 9046-40-6, Pectic acid 9057-02-7, Pullulan 9060-75-7D, Arabinan, derivs. 9072-19-9, Fucoidan 20064-29-3, Trimethylammonium propane 24305-42-8, Triethylammonium propane 24529-88-2 25322-68-3D, derivs. 37331-28-5, Pustulan 60495-58-1, Galactocarolose 64612-25-5D, Fucan, derivs. 68354-92-7 69992-87-6, Keratan 73294-85-6 75634-40-1, Dermatan 76822-97-4

78543-25-6 83554-62-5 106392-12-5D, Pluronic, derivs. 108032-13-9
115534-33-3, Tmadph 124050-77-7, Transfectam 124076-29-5 127512-30-5
128835-92-7, Lipofectin **132172-61-3** 137056-72-5,
DC-Chol **144189-73-1**, Dotap 145310-87-8, Transfectace
153312-64-2, DMRIE **158571-62-1**, Lipofectamine
161293-59-0 161441-83-4 183283-19-4, Edmpc 186198-32-3
199171-54-5, DLRIE 201491-17-0, Cytofectin **208040-06-6**
, GAP-DLRIE 225940-35-2, glycero-3-Ethylphosphatidylcholine
282533-23-7, Dospa 303097-27-0 303097-29-2 303097-31-6
303097-33-8 303097-35-0

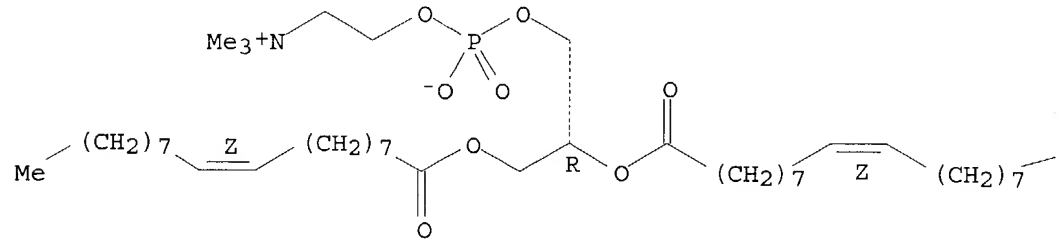
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug carrier; peptide compns. useful for delivering anti-inflammatory agents into a cell)

IT **4235-95-4**, Dopc **128835-92-7**, Lipofectin
132172-61-3 144189-73-1, Dotap **153312-64-2**,
DMRIE **158571-62-1**, Lipofectamine **199171-54-5**, DLRIE
208040-06-6, GAP-DLRIE **282533-23-7**, Dospa
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug carrier; peptide compns. useful for delivering anti-inflammatory agents into a cell)

RN 4235-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

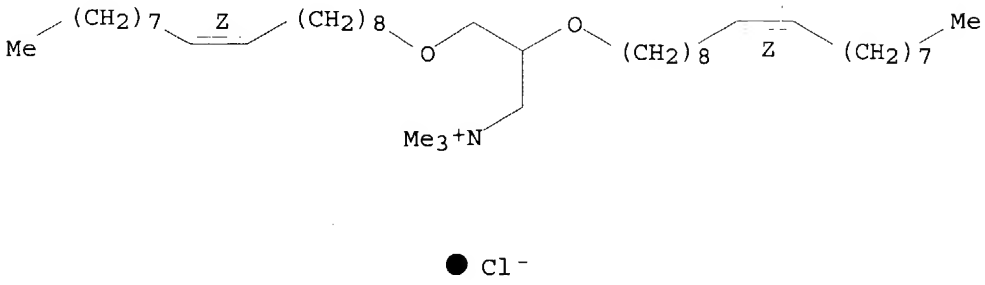
Me

RN 128835-92-7 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 104162-48-3
CMF C42 H84 N O2 . Cl

Double bond geometry as shown.

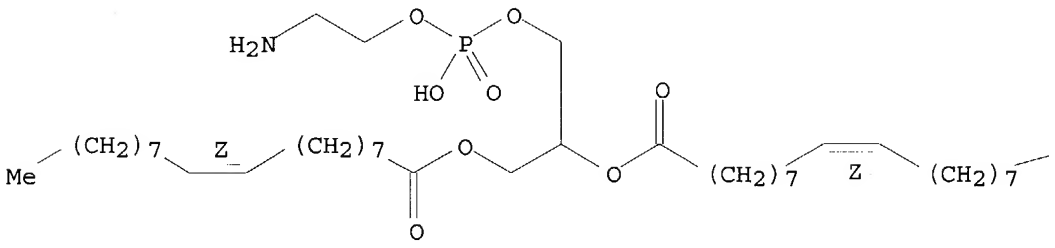


CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



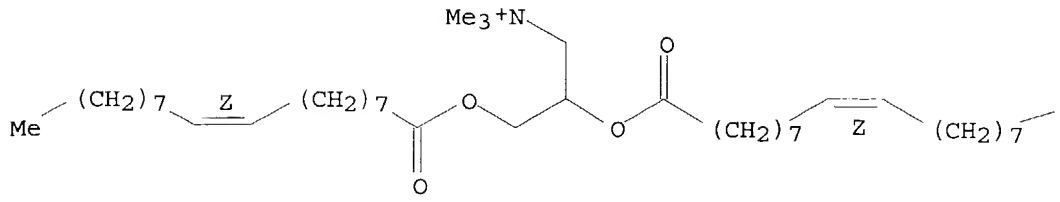
PAGE 1-B

Me

RN 132172-61-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



● Cl^-

PAGE 1-B

Me

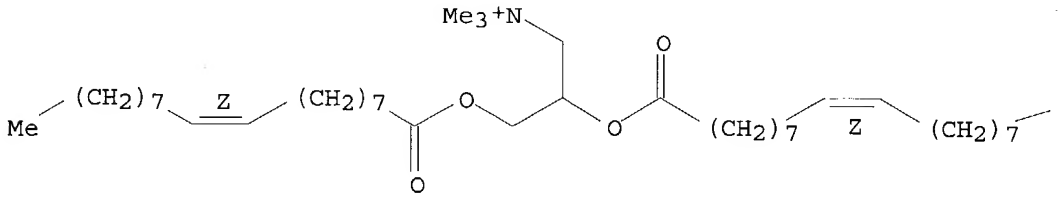
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



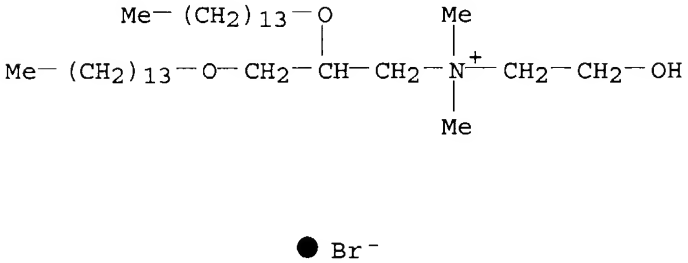
PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

RN 153312-64-2 HCAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



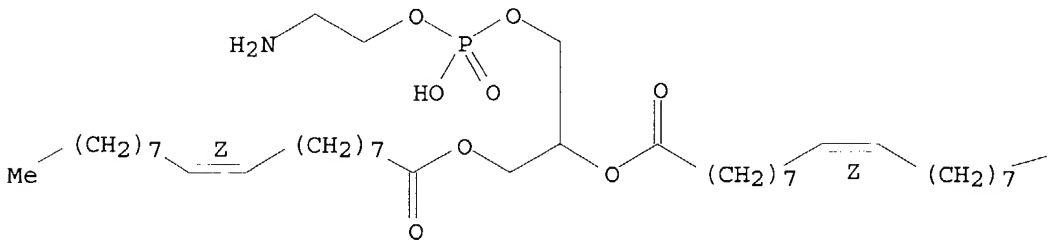
RN 158571-62-1 HCAPLUS
CN 1-Propanaminium, N-[3-[[3-[[4-[(3-aminopropyl)amino]butyl]amino]propyl]amino]-3-oxopropyl]-N,N-dimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, salt with trifluoroacetic acid (1:1), mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

CM 2

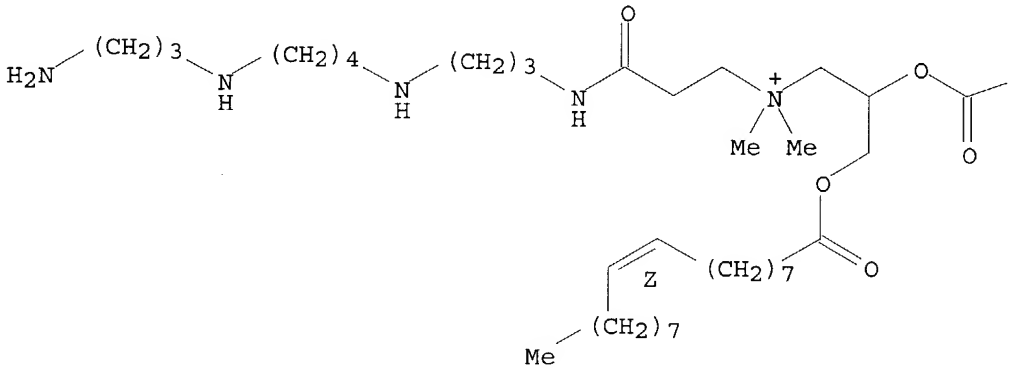
CRN 185097-43-2
CMF C54 H106 N5 O5 . C2 F3 O2

CM 3

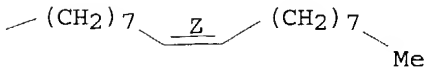
CRN 181508-68-9
CMF C54 H106 N5 O5

Double bond geometry as shown.

PAGE 1-A

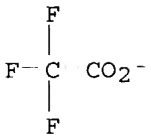


PAGE 1-B

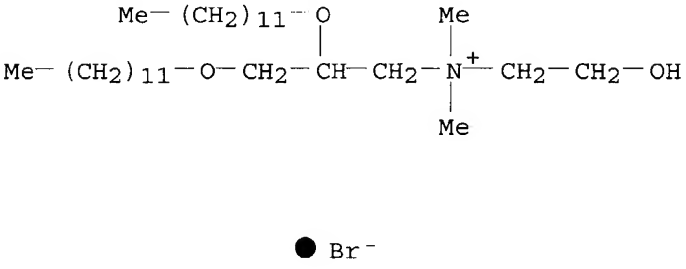


CM 4

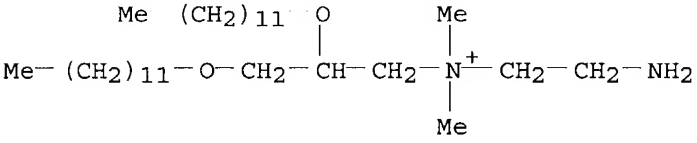
CRN 14477-72-6
CMF C2 F3 O2



RN 199171-54-5 HCAPLUS
CN 1-Propanaminium, 2,3-bis(dodecyloxy)-N-(2-hydroxyethyl)-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)



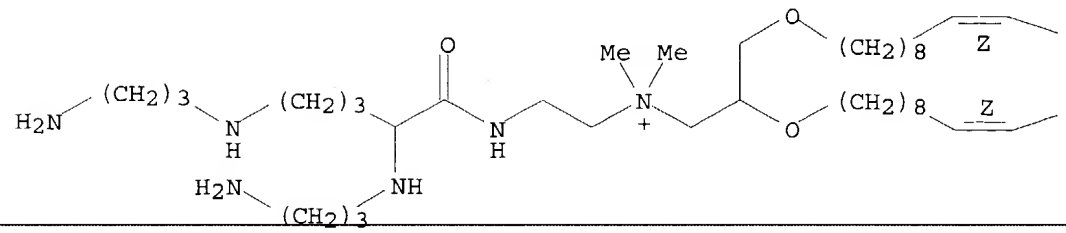
RN 208040-06-6 HCAPLUS
CN 1-Propanaminium, N-(2-aminoethyl)-2,3-bis(dodecyloxy)-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)



RN 282533-23-7 HCAPLUS
CN 1-Propanaminium, N-[2-[[2,5-bis[(3-aminopropyl)amino]-1-oxopentyl]amino]ethyl]-N,N-dimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride, tetrahydrochloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

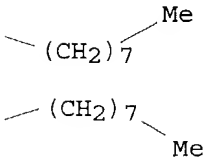
PAGE 1-A



● Cl⁻

● 4 HCl

PAGE 1-B



L52 ANSWER 35 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:552713 HCAPLUS
DOCUMENT NUMBER: 134:1122
TITLE: Gene delivery for genetically engineered mucosal cells with enhanced function
AUTHOR(S): Nagatani, Naoki; Shinkai, Masashige; Nagase, Yayoi; Honda, Hiroyuki; Hata, Ken-Ichiro; Mizuno, Hirokazu; Ueda, Minoru; Kobayashi, Takeshi
CORPORATE SOURCE: Department of Biotechnology, Graduate School of Engineering, Nagoya University, Nagoya, 464-8603, Japan
SOURCE: Biotechnology Letters (2000), 22(12), 999-1002
CODEN: BILED3; ISSN: 0141-5492
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A non-viral transfection method for oral mucosal cells was investigated using a modified transfection method and five com. transfection reagents. The CellFECTIN gave the highest expression of a transfected gene. When the mucosal cells were transfected with 0.3 ng DNA/cell, the transfection efficiency was optimal, and the production of a reporter protein increased up to ten times higher than those with the other transfection reagents.

CC 3-2 (Biochemical Genetics)

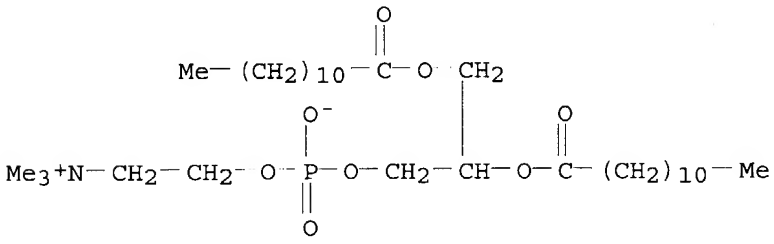
Section cross-reference(s): 1, 14

IT **Drug delivery systems**
(**oral**; gene delivery for genetically engineered mucosal cells with enhanced function)

IT 2462-63-7, Dioleoyl phosphatidylethanolamine **18656-40-1**, Dilauroyl phosphatidylcholine **128835-92-7**, LipoFECTIN 131897-06-8, N-(α-Trimethylammonio-acetyl)-didodecyl-D-glutamate chloride **158571-62-1**, LipofectAMINE 189203-04-1, CellFECTIN **189203-05-2**, DMRIE-C 213252-23-4, SuperFect
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene delivery for genetically engineered mucosal cells with enhanced function)

IT **18656-40-1**, Dilauroyl phosphatidylcholine **128835-92-7**, LipoFECTIN **158571-62-1**, LipofectAMINE **189203-05-2**, DMRIE-C
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene delivery for genetically engineered mucosal cells with enhanced function)

RN 18656-40-1 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheneicosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxododecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

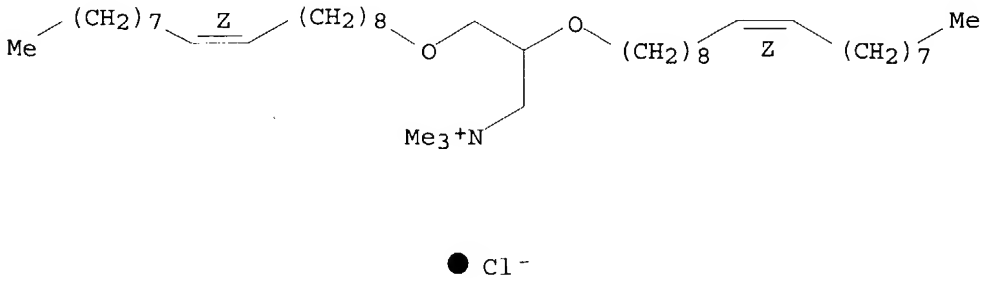


RN 128835-92-7 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 104162-48-3
CMF C42 H84 N O2 . Cl

Double bond geometry as shown.

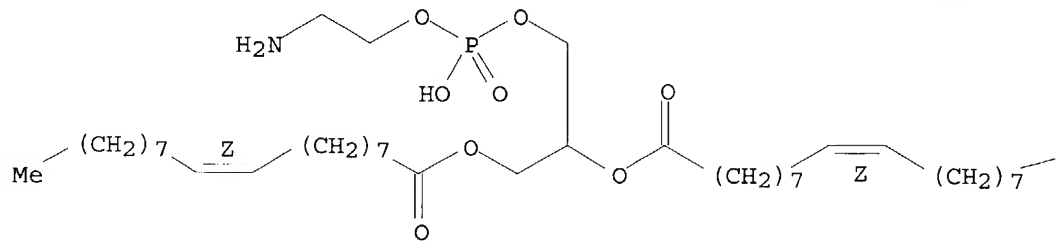


CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

~~PAGE 1-A~~



PAGE 1-B

Me

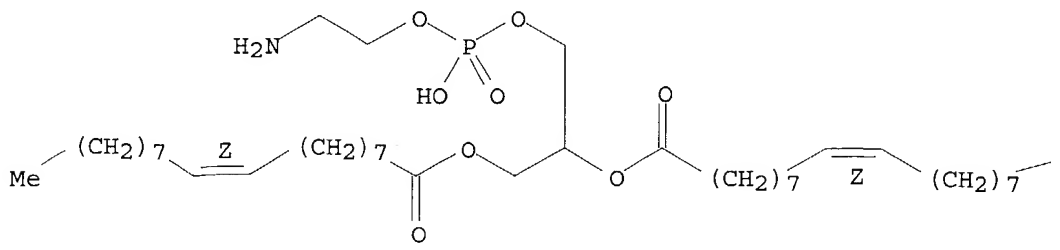
RN 158571-62-1 HCAPLUS
CN 1-Propanaminium, N-[3-[[3-[[4-[(3-aminopropyl)amino]butyl]amino]propyl]amino]-3-oxopropyl]-N,N-dimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, salt with trifluoroacetic acid (1:1), mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

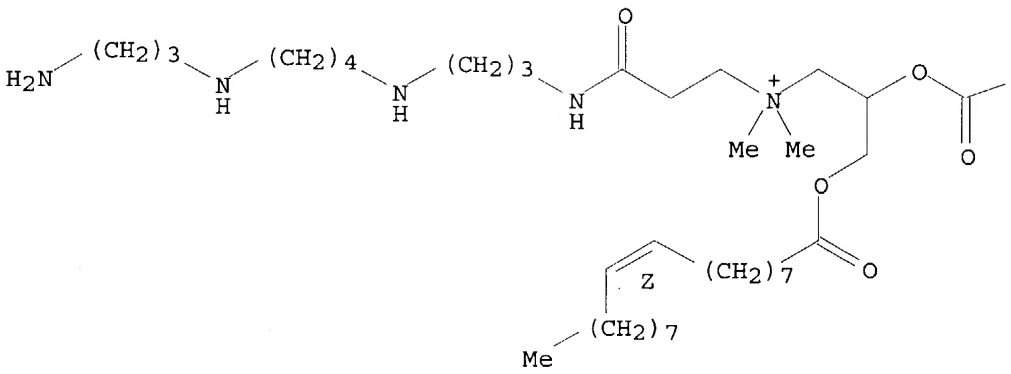
CRN 185097-43-2
CMF C54 H106 N5 O5 . C2 F3 O2

CM 3

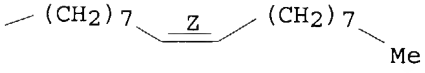
CRN 181508-68-9
CMF C54 H106 N5 O5

Double bond geometry as shown.

PAGE 1-A

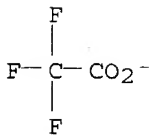


PAGE 1-B



CM 4

CRN 14477-72-6
CMF C2 F3 O2

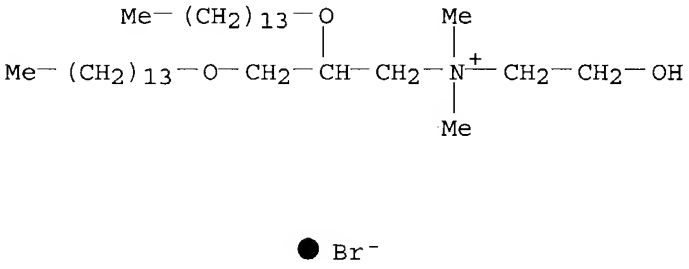


RN 189203-05-2 HCAPLUS

CN Cholest-5-en-3-ol (3β)-, mixt. with N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-1-propanaminium bromide (9CI) (CA INDEX NAME)

CM 1

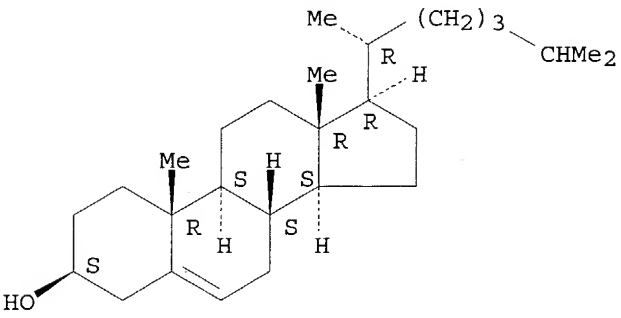
CRN 153312-64-2
CMF C35 H74 N O3 . Br



CM 2

CRN 57-88-5
CMF C27 H46 O

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 36 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:335212 HCAPLUS
DOCUMENT NUMBER: 132:339369

TITLE: An inhalation system containing a lipid mixture
INVENTOR(S): Pilkiewicz, Frank G.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027359	A1	20000518	WO 1999-US26858	19991112
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1128813	A1	20010905	EP 1999-958945	19991112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002529393	T2	20020910	JP 2000-580590	19991112
NZ 511568	A	20030829	NZ 1999-511568	19991112
AU 766703	B2	20031023	AU 2000-16212	19991112
ZA 2001003645	A	20020805	ZA 2001-3645	20010504

PRIORITY APPLN. INFO.:
US 1998-108067P P 19981112
US 1998-108126P P 19981112
WO 1999-US26858 W 19991112

AB A system for administering a bioactive agent by inhalation comprises a lipid mixture containing a phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol, phosphatidylinositol, sterol, albumin and phosphatidic acid in various combinations and ratios. The biol. active agent is a drug, such as antitumor or antimicrobial agent, a compound affecting endocrine function, an antibody, a gene, a cytokine, a differentiating agent, etc.

IC ICM A61K009-127
ICS A61K009-12

CC 63-6 (Pharmaceuticals)

IT **cDNA**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for α1-antitrypsin or CFTR; inhalation system containing lipid mixture for therapy)

IT **Drug delivery systems**
(inhalants; inhalation system containing lipid mixture for therapy)

IT Adrenoceptor antagonists
Analgesics
Anaphylaxis
Anti-AIDS agents
Anti-infective agents
Anti-inflammatory agents
Antiarrhythmics
Antiasthmatics
Antibacterial agents

Anticoagulants
Antidiabetic agents
Antiemetics
Antihypertensives
Antitussives
Antiviral agents
Cardiovascular agents
Cholinergic antagonists
Cystic fibrosis
Emphysema
Fungicides
Human immunodeficiency virus 1
Immunosuppressants
Opioid antagonists
Platelet aggregation inhibitors
Tuberculostatics
Vaccines
Vasodilators
(inhalation system containing lipid mixture for therapy)

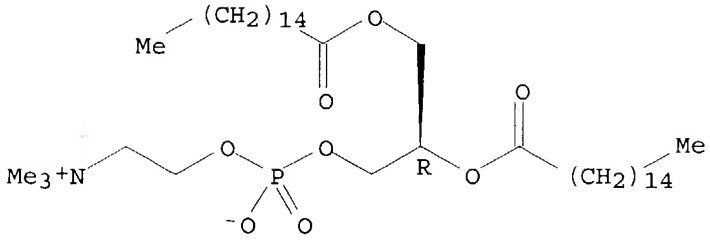
IT Anthracyclines
Antibodies
Cannabinoids
Corticosteroids, biological studies
Cytokines
DNA
Gene, animal
Hormones, animal, biological studies
Immunoglobulins
Interferons
Opioids
Peptides, biological studies
Proteins, general, biological studies
RNA
Retinoids
Sulfonamides
Tetracyclines
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhalation system containing lipid mixture for therapy)

IT 57-88-5, Cholesterol, biological studies **63-89-8**, Dipalmitoylphosphatidylcholine 2462-63-7, DOPE 4537-77-3, DPPG 61361-72-6, Dimyristoylphosphatidylglycerol **144189-73-1**, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhalation system containing lipid mixture for therapy)

IT **63-89-8**, Dipalmitoylphosphatidylcholine **144189-73-1**, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhalation system containing lipid mixture for therapy)

RN 63-89-8 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



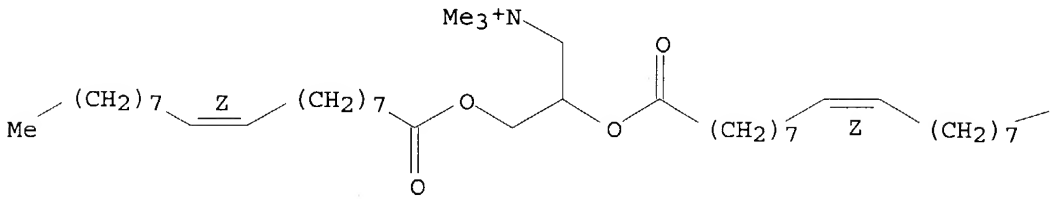
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO_3^-

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 37 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:216866 HCAPLUS
DOCUMENT NUMBER: 133:79118
TITLE: Electroporation-enhanced gene delivery in mammary tumors
AUTHOR(S): Wells, J. M.; Li, L. H.; Sen, A.; Jahreis, G. P.; Hui, S. W.
CORPORATE SOURCE: Membrane Biophysics Laboratory, Molecular and Cellular Biophysics Department, Roswell Park Cancer Institute, Buffalo, NY, 14263-0001, USA
SOURCE: Gene Therapy (2000), 7(7), 541-547
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Electroporation was applied to enhance gene transfer into s.c. MC2 murine breast tumors. Cultured MC2 cells were also transfected by electroporation or by cationic liposomes in the presence of serum using pSV-luc plasmids. Electroporation parameters and liposome formulation were optimized to achieve the highest relative levels of transfection. An elec. field threshold for successful electrotransfection in cultured cells appeared around 800-900 V/cm. The liposomes used contained the cationic lipid dioleoyl-3-trimethylammonium propane (DOTAP). Multilamellar vesicles (MLV) had a 10-fold advantage over small unilamellar vesicles (SUV) in cell culture transfection. For in vivo gene delivery, the plasmids were injected either alone, or in complex with MLV or SUV DOTAP liposomes. A series of six elec. pulses 1 ms long were applied across tumors, using caliper electrodes on the skin surface. Elec. field strengths ranged from 400-2300 V/cm. Luciferase expression was approx. two orders of magnitude higher than controls in tumors treated with pulses ≥800 V/cm. Differences between enhanced relative levels of transfection using uncomplexed plasmid and lipoplexes were not statistically significant. Distribution of DNA into tumor tissues was monitored by fluorescence in situ PCR. The highest nos. of fluorescent cells were found in tumors electroporated following the injection of plasmid. The significant transfection improvement shows that in vivo electroporation is a powerful tool for local gene delivery to tumors.

CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 1, 3

IT Electroporation
Gene therapy
Plasmids
Transformation, genetic
(electroporation-enhanced gene delivery to solid tumors)

IT **Drug delivery systems**
(liposomes; electroporation-enhanced gene delivery to solid tumors)

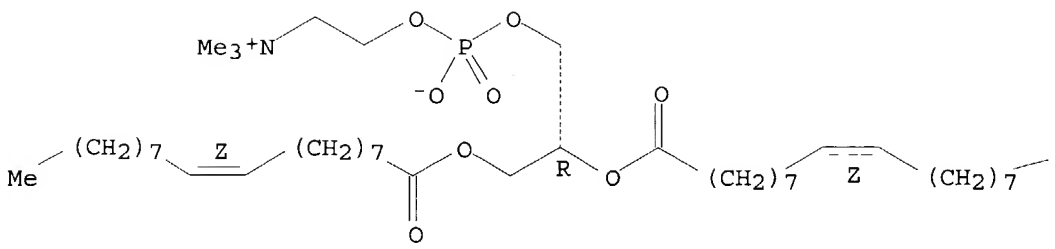
IT **4235-95-4 144189-73-1**, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(electroporation-enhanced gene delivery to solid tumors)

IT **4235-95-4 144189-73-1**, DOTAP
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(electroporation-enhanced gene delivery to solid tumors)

RN 4235-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

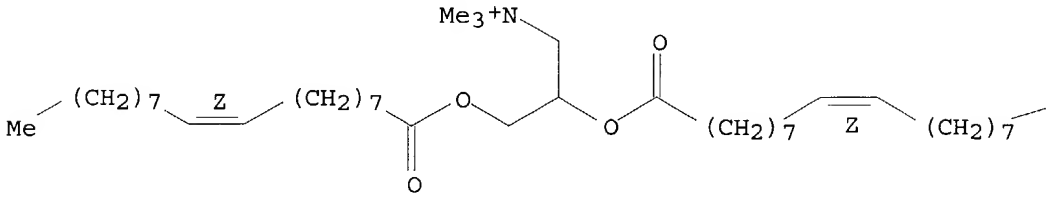
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO_3^-

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 38 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:98268 HCAPLUS
DOCUMENT NUMBER: 132:156844
TITLE: Lipid emulsion and solid lipid nanoparticle as a gene or drug carrier
INVENTOR(S): Jeong, Seo Young; Kwon, Ick Chan; Chung, Hesson
PATENT ASSIGNEE(S): Korea Institute of Science and Technology, S. Korea
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006120	A1	20000210	WO 1999-KR414	19990730
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9950689	A1	20000221	AU 1999-50689	19990730
KR 2000012106	A	20000225	KR 1999-31339	19990730
EP 1100464	A1	20010523	EP 1999-935145	19990730
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002521423	T2	20020716	JP 2000-561977	19990730

PRIORITY APPLN. INFO.: KR 1998-31249 A 19980731
WO 1999-KR414 W 19990730

AB The present invention relates to oil-in-water lipid emulsions composed of non-triglyceride oils and solid lipid nanoparticles (SLN) composed of triglyceride or Et stearate used as gene transfection agents and drug delivery systems and method for preparing thereof. The present invention also concerns the method of transferring genes or drugs efficiently into cells by using the lipid emulsions and solid lipid nanoparticles. Also the present invention relates to the method of preparing lipid emulsions containing lipophilic or amphiphilic drugs by using squalene or squalane as the core oil. The present invention also concerns the method of preparing the solid lipid nanoparticles containing lipophilic or amphiphilic drugs by using Et stearate as the core fat.

IC ICM A61K009-107

CC 63-6 (Pharmaceuticals)
IT **Nucleic acids**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antisense; lipid emulsion and solid lipid nanoparticle as gene or drug carrier)
IT **Drug delivery systems**
(injections, i.m.; lipid emulsion and solid lipid nanoparticle as gene or drug carrier)
IT **Drug delivery systems**
(injections, i.v.; lipid emulsion and solid lipid nanoparticle as gene or drug carrier)
IT **Drug delivery systems**
(injections, s.c.; lipid emulsion and solid lipid nanoparticle as gene or drug carrier)
IT **Drug delivery systems**
(intratracheal; lipid emulsion and solid lipid nanoparticle as gene or drug carrier)
IT Adrenoceptor antagonists
Analgesics
Anesthetics
Antibiotics
Anticonvulsants
Antidepressants
Antitumor agents
Antiviral agents
Anxiolytics
Cholinergic agonists
Drug targeting
Emulsifying agents
Fungicides
Gene targeting
Immunostimulants
Immunosuppressants
Ribosome
Transformation, genetic
(lipid emulsion and solid lipid nanoparticle as gene or drug carrier)
IT Antibodies
Bile salts
DNA
Estrogens
Fats and Glyceridic oils, biological studies
Glycolipids
Glycosaminoglycans, biological studies
Histones
Hormones, animal, biological studies
Lipopeptides
Oligonucleotides
Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphatidylserines
Phospholipids, biological studies
Polynucleotides
Polyoxyalkylenes, biological studies
Prostaglandins
RNA
Vitamins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid emulsion and solid lipid nanoparticle as gene or drug carrier)
IT **Drug delivery systems**

(nasal; lipid emulsion and solid lipid nanoparticle as gene or drug carrier)

IT **Plasmids**
(pCMV; lipid emulsion and solid lipid nanoparticle as gene or drug carrier)

IT **Drug delivery systems**
(parenterals; lipid emulsion and solid lipid nanoparticle as gene or drug carrier)

IT **Drug delivery systems**
(topical; lipid emulsion and solid lipid nanoparticle as gene or drug carrier)

IT 56-81-5, 1,2,3-Propanetriol, biological studies 57-83-0, Progesterone, biological studies 57-88-5, Cholesterol, biological studies 107-64-2, Dimethyldioctadecylammonium chloride 111-01-3, Squalane 111-02-4, Squalene 111-61-5, Ethyl stearate 302-79-4, Retinoic acid 538-24-9, Trilaurin 4004-05-1 **4235-95-4** 9005-65-6, Tween 80 13292-46-1, Rifampicin 15307-79-6, Diclofenac sodium 25104-18-1, Polylysine 25322-68-3 25637-84-7, Diolein 25805-17-8, Polyethyloxazoline 35121-78-9, Prostacyclin 38000-06-5, Polylysine 59865-13-3, Cyclosporin A 72719-84-7 96326-74-8 **113669-21-9** 121315-93-3 **132172-61-3 138915-91-0**, 1,2-Dipalmitoyl-3-trimethylammoniopropane **173666-09-6** 257637-27-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid emulsion and solid lipid nanoparticle as gene or drug carrier)

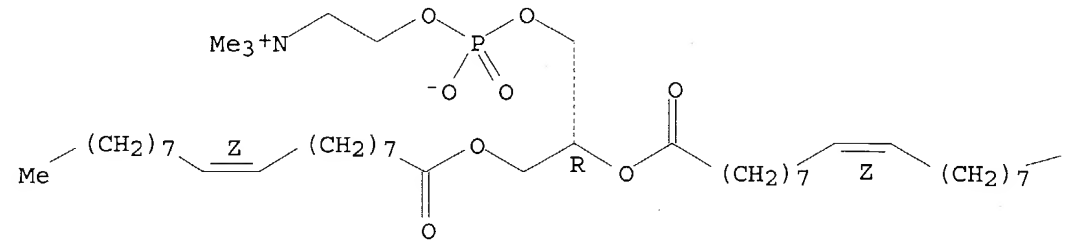
IT **4235-95-4 113669-21-9 132172-61-3 138915-91-0**, 1,2-Dipalmitoyl-3-trimethylammoniopropane **173666-09-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid emulsion and solid lipid nanoparticle as gene or drug carrier)

RN 4235-95-4 HCAPLUS

CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



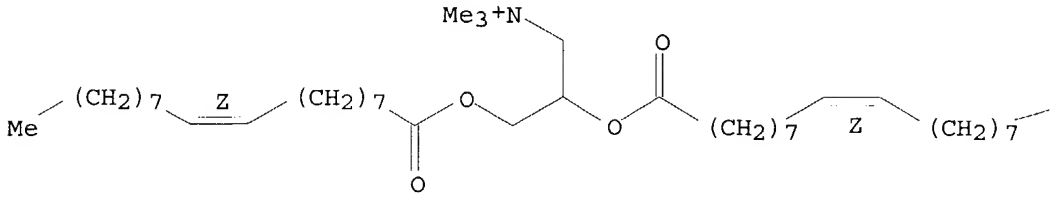
PAGE 1-B

Me

RN 113669-21-9 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



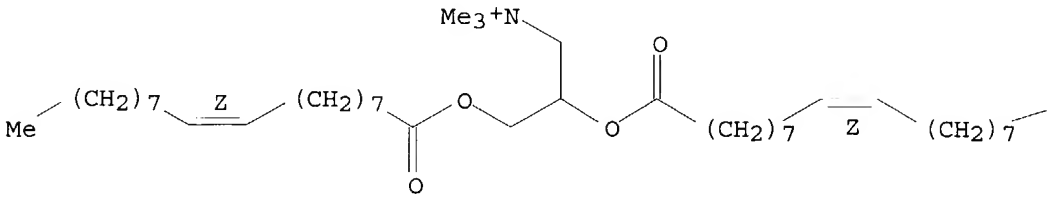
PAGE 1-B

Me

RN 132172-61-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-,
chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

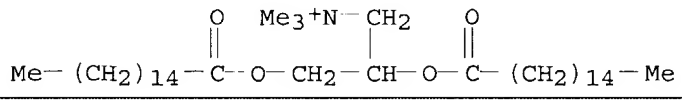


● Cl⁻

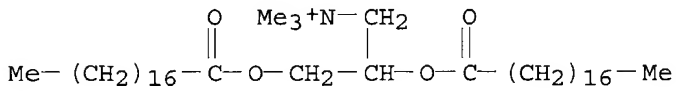
PAGE 1-B

Me

RN 138915-91-0 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(1-oxohexadecyl)oxy]- (9CI) (CA INDEX NAME)



RN 173666-09-6 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 39 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:95759 HCAPLUS
DOCUMENT NUMBER: 132:325932
TITLE: Calcium enhances the transfection potency of plasmid DNA-cationic liposome complexes
AUTHOR(S): Lam, A. M. I.; Cullis, P. R.
CORPORATE SOURCE: Faculty of Medicine, Department of Biochemistry and Molecular Biology, University of British Columbia, Vancouver, BC, Can.
SOURCE: Biochimica et Biophysica Acta (2000), 1463(2), 279-290
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It is shown that calcium increases the in vitro transfection potency of plasmid DNA-cationic liposome complexes from 3- to 20-fold. The effect is Ca2+ specific as other cations, such as Mg2+ and Na+, do not give rise to enhanced transfection and the effect can be inhibited by the presence of EGTA. It is shown that Ca2+ increases cellular uptake of the DNA-lipid complexes, indicating that increased transfection potency arises from increased intracellular delivery of both cationic lipid and plasmid DNA in the presence of Ca2+. In particular, it is shown that the levels of intact intracellular plasmid DNA are significantly enhanced when Ca2+ is present. The generality of the Ca2+ effect for enhancing complex-mediated transfection is demonstrated for a number of different cell lines and different cationic lipid formulations. It is concluded that addition of Ca2+ represents a simple and useful protocol for enhancing in vitro transfection properties of plasmid DNA-cationic lipid complexes.
CC 63-5 (Pharmaceuticals)
IT **Plasmids**
Transformation, genetic
(calcium enhances the transfection potency of plasmid DNA-cationic liposome complexes)

IT **DNA**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(complexes; calcium enhances the transfection potency of plasmid DNA-cationic liposome complexes)

IT **Drug delivery systems**
(liposomes; calcium enhances the transfection potency of plasmid DNA-cationic liposome complexes)

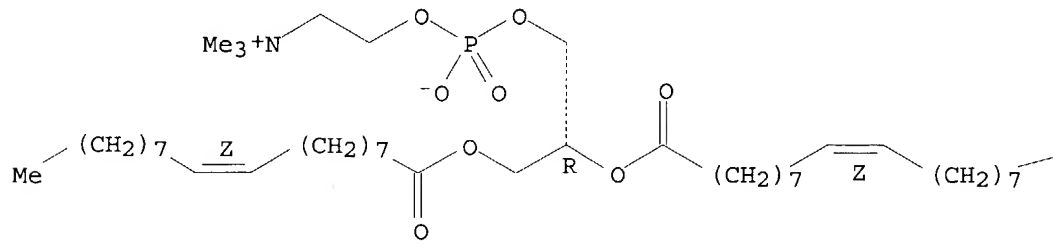
IT 67-42-5, Egta 107-64-2, Dimethyldistearylammonium chloride 3700-67-2, Dimethyldioctadecylammonium bromide 4004-05-1, Dope **4235-95-4** 7212-69-3, Dodac 7440-70-2, Calcium, biological studies 10043-52-4, Calcium chloride, biological studies **104162-48-3**, Dotma
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(calcium enhances the transfection potency of plasmid DNA-cationic liposome complexes)

IT **4235-95-4 104162-48-3**, Dotma
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(calcium enhances the transfection potency of plasmid DNA-cationic liposome complexes)

RN 4235-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A

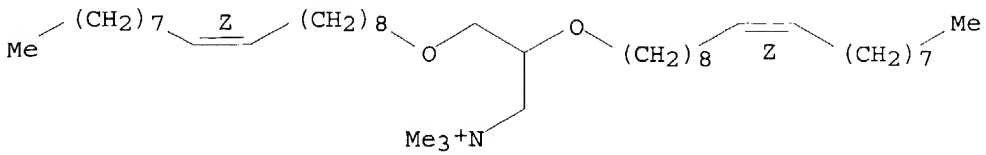


PAGE 1-B

Me

RN 104162-48-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● Cl^-

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 40 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:14945 HCAPLUS
DOCUMENT NUMBER: 132:83648
TITLE: Macromolecule-lipid complexes and methods for making and using
INVENTOR(S): Safinya, Cyrus R.; Raedler, Joachim Oskar; Koltover, Ilya
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000033	A1	20000106	WO 1999-US13982	19990621
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6358523	B1	20020319	US 1998-105571	19980626
AU 9947030	A1	20000117	AU 1999-47030	19990621

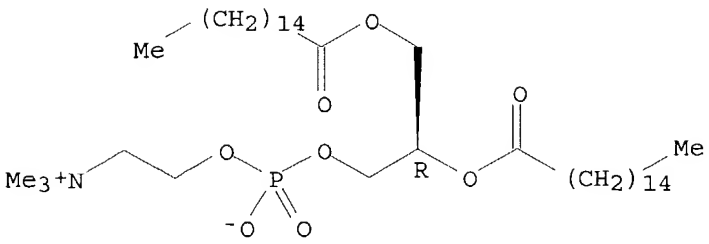
PRIORITY APPLN. INFO.:

US 1998-105571	A	19980626
US 1996-32163P	P	19961206
US 1997-985625	A2	19971205
WO 1999-US13982	W	19990621

AB The invention provides novel compns. involving macromol.-lipid complexes and methods for making them. These compns. and methods of the invention are significant improvements in the field of macromol.-lipid complex processing, macromol. targeting and delivery to various biol. systems. Cationic liposome complexed with DNA were prepared using DOTAP/dioleoylphosphatidylcholine or DOTAP/dioleoylphosphatidylethanolamine.

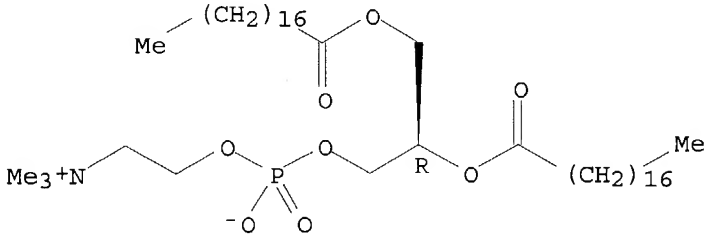
IC ICM A01N063-00
ICS A61K009-127; G01N033-92; C07H021-04
CC 63-6 (Pharmaceuticals)
IT **DNA**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(complexes; cationic liposome-DNA complexes)
IT **Drug delivery systems**
(liposomes; cationic liposome-DNA complexes)
IT **63-89-8**, Dipalmitoylphosphatidylcholine **816-94-4**, Distearoylphosphatidylcholine 923-61-5 **998-06-1** 998-07-2 1069-79-0 **2701-19-1 3355-26-8 3355-27-9 3436-44-0** 4004-05-1, Dope **4235-95-4**, Dopc 5634-86-6 **17688-29-8**, Diarachidonoylphosphatidylcholine **18194-24-6**, Dimyristoylphosphatidylcholine **18194-25-7**, Dilauroylphosphatidylcholine **19191-91-4** 19805-18-6 20707-71-5 **27869-45-0 27869-47-2 34506-67-7** 34813-40-6 **37070-48-7 39036-04-9 51779-95-4 51779-96-5 56391-91-4 56750-90-4 56782-46-8 56815-99-7 56816-00-3** 59752-57-7 **61596-53-0** 61599-23-3 **66414-33-3 66414-34-4**, Divaleroylphosphatidylcholine **70897-27-7 71242-28-9 72719-83-6** 72719-84-7 **76733-52-3** 87250-80-4 **91742-11-9 95416-27-6** 96326-74-8 96760-44-0 96893-06-0 109032-52-2 **112241-60-8** 121315-93-3 127512-29-2 **137133-79-0 138915-91-0 144189-73-1**, Dotap **173666-09-6** 183317-85-3 201036-16-0 207131-40-6 217075-01-9 253685-27-7 **253685-28-8**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic liposome-DNA complexes)
IT **63-89-8**, Dipalmitoylphosphatidylcholine **816-94-4**, Distearoylphosphatidylcholine **998-06-1 2701-19-1 3355-26-8 3355-27-9 3436-44-0 4235-95-4**, Dopc **17688-29-8**, Diarachidonoylphosphatidylcholine **18194-24-6**, Dimyristoylphosphatidylcholine **18194-25-7**, Dilauroylphosphatidylcholine **19191-91-4 27869-45-0 27869-47-2 34506-67-7 37070-48-7 39036-04-9 51779-95-4 51779-96-5 56391-91-4 56750-90-4 56782-46-8 56815-99-7 56816-00-3 61596-53-0 66414-33-3 66414-34-4**, Divaleroylphosphatidylcholine **70897-27-7 71242-28-9 72719-83-6 76733-52-3 91742-11-9 95416-27-6 112241-60-8 137133-79-0 138915-91-0 144189-73-1**, Dotap **173666-09-6 253685-28-8**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic liposome-DNA complexes)
RN 63-89-8 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 816-94-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

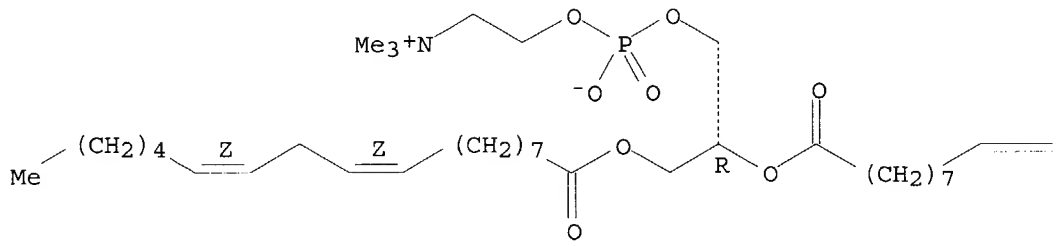
Absolute stereochemistry.



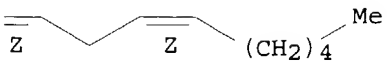
RN 998-06-1 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosa-18,21-dien-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z,12Z)-1-oxo-9,12-octadecadienyl]oxy]-, inner salt, 4-oxide, (7R,18Z,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



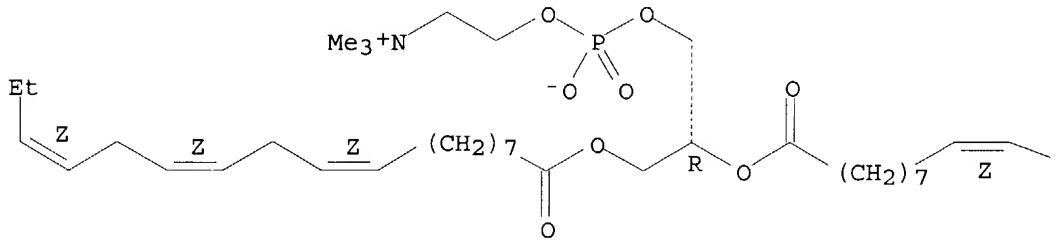
PAGE 1-B



RN 2701-19-1 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosa-18,21,24-trien-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z,12Z,15Z)-1-oxo-9,12,15-octadecatrienyl]oxy]-, inner salt, 4-oxide, (7R,18Z,21Z,24Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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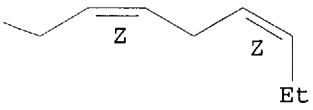
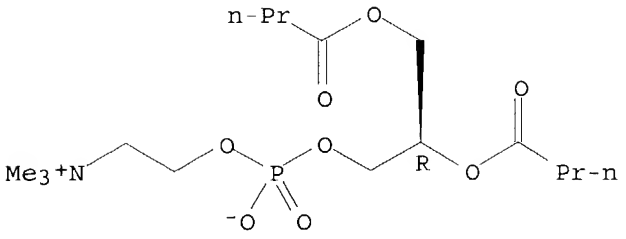


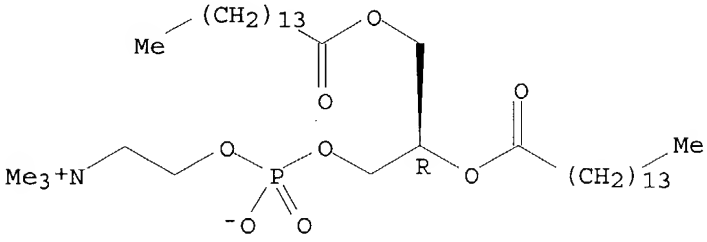
RN 3355-26-8 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatridecan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-(1-oxobutoxy)-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



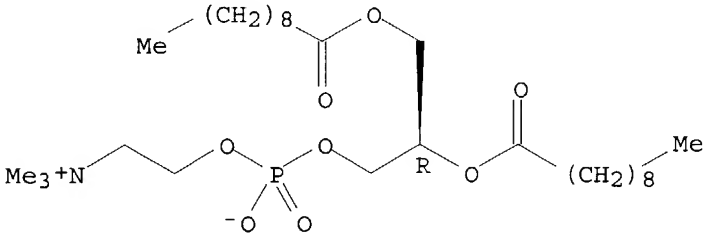
RN 3355-27-9 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatetracosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxopentadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 3436-44-0 HCAPLUS
CN 3,5,9-Trioxa-4-phosphanonadecan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxodecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

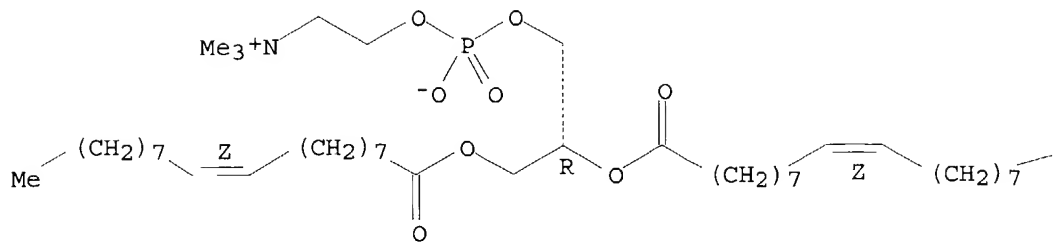
Absolute stereochemistry.



RN 4235-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A

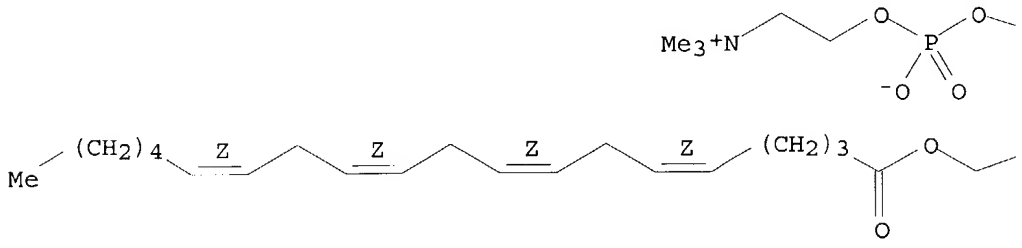


PAGE 1-B

RN 17688-29-8 HCAPLUS
CN 3,5,9-Trioxa-4-phosphanonacosa-14,17,20,23-tetraen-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(5Z,8Z,11Z,14Z)-1-oxo-5,8,11,14-eicosatetraenyl]oxy]-, inner salt, 4-oxide, (7R,14Z,17Z,20Z,23Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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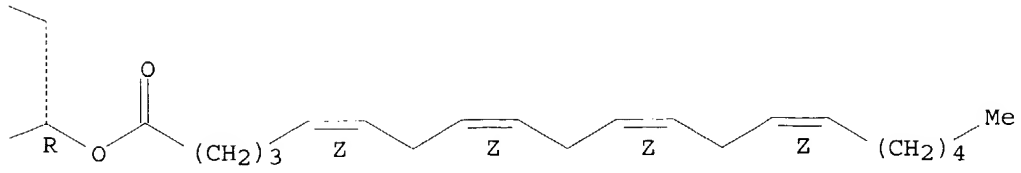
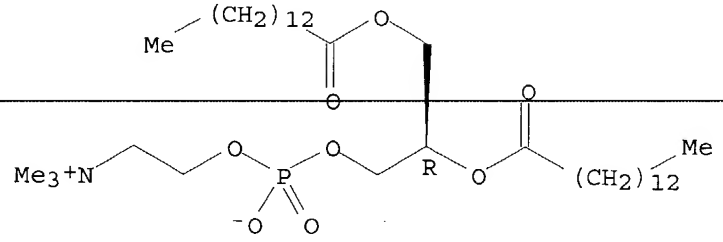


RN 18194-24-6 HCAPLUS

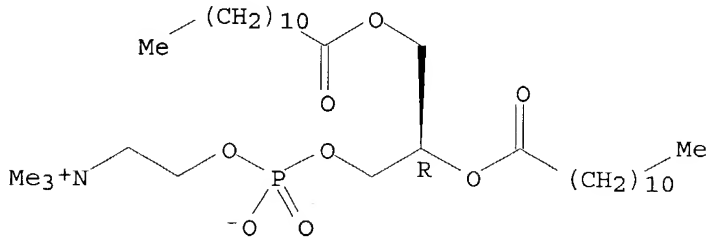
CN 3,5,9-Trioxa-4-phosphatricosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxotetradecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



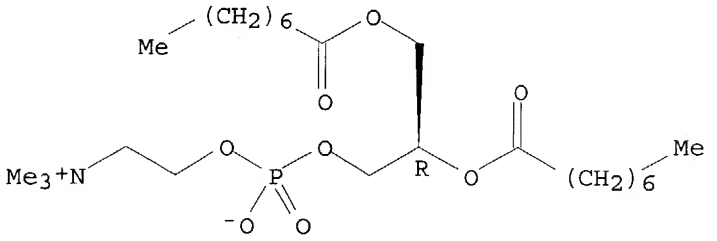
RN 18194-25-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheneicosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxododecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



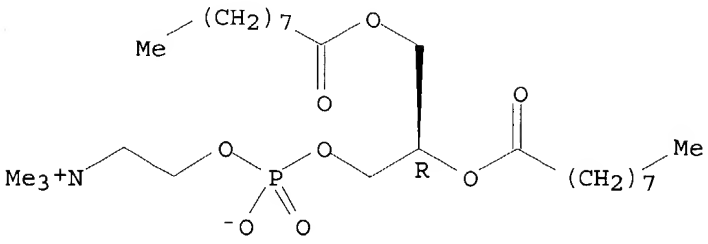
RN 19191-91-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptadecan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



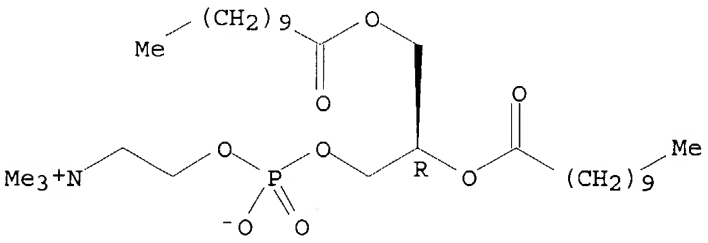
RN 27869-45-0 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaoctadecan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxononyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



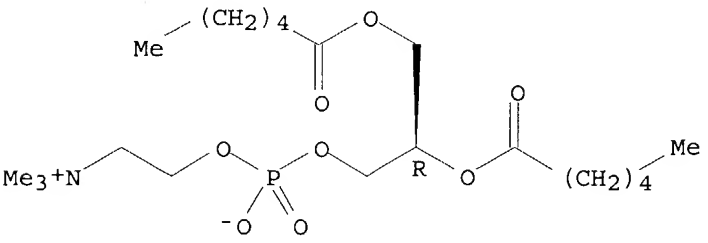
RN 27869-47-2 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaeicosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxoundecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



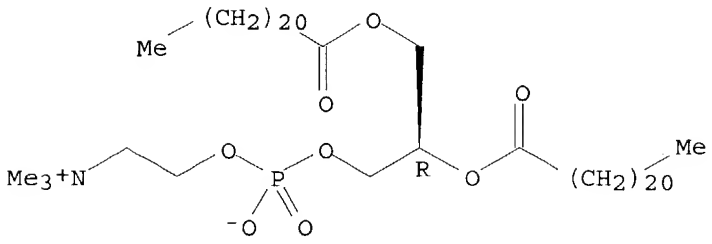
RN 34506-67-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentadecan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 37070-48-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphahentriacontan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxodocosyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 39036-04-9 HCAPLUS
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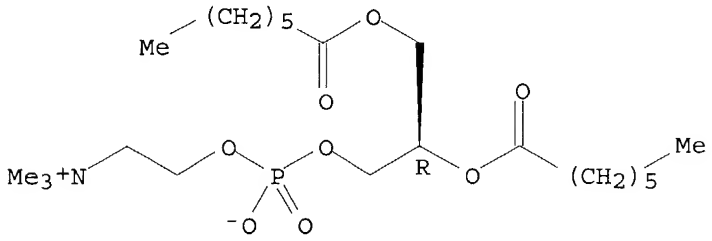
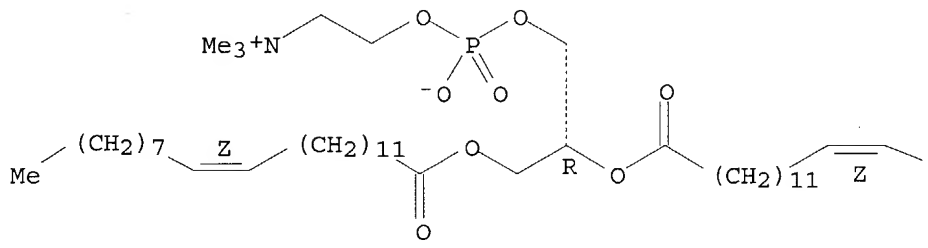
Absolute stereochemistry.



RN 51779-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphahentriacont-22-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(13Z)-1-oxo-13-docosenyl]oxy]-, inner salt, 4-oxide, (7R,22Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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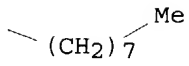
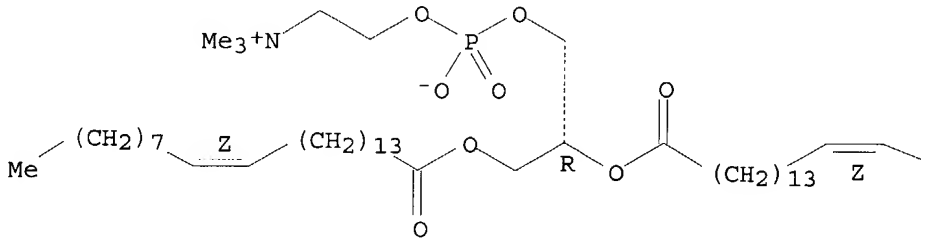


RN 51779-96-5 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatritriacont-24-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(15Z)-1-oxo-15-tetracosenyl]oxy]-, inner salt, 4-oxide, (7R,24Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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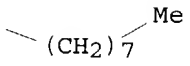
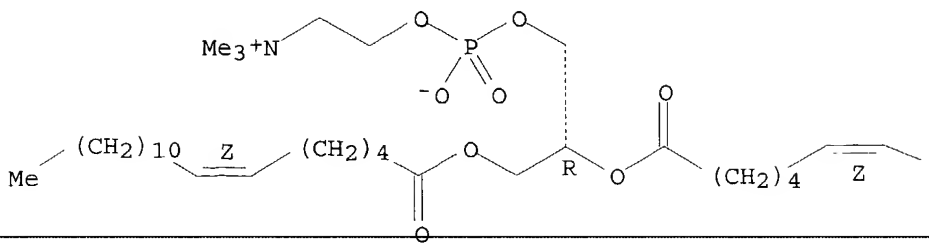


RN 56391-91-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-15-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(6Z)-1-oxo-6-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,15Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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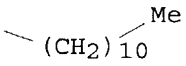

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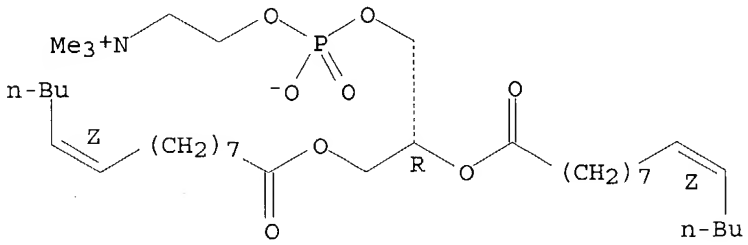
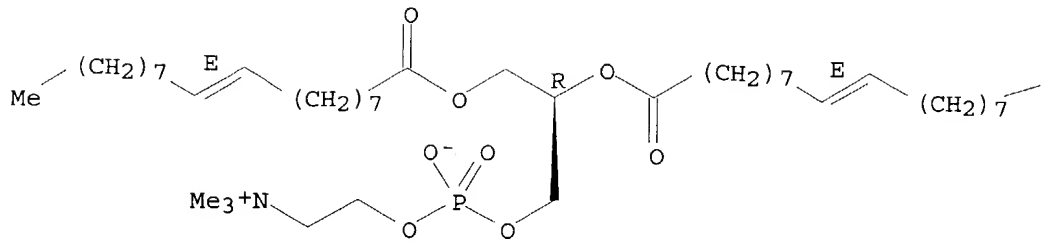
Absolute stereochemistry.
Double bond geometry as shown.



RN 56782-46-8 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9E)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



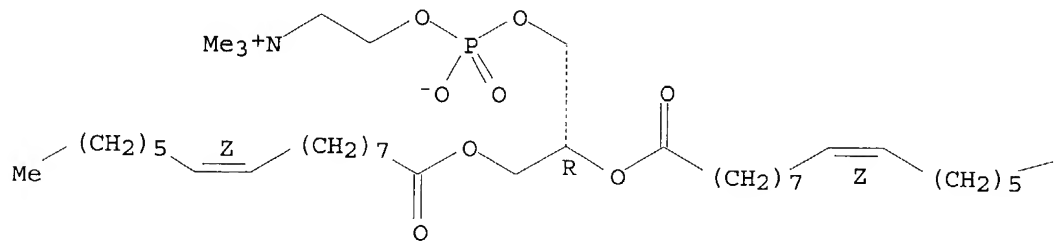
PAGE 1-B

Me

RN 56815-99-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-hexadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



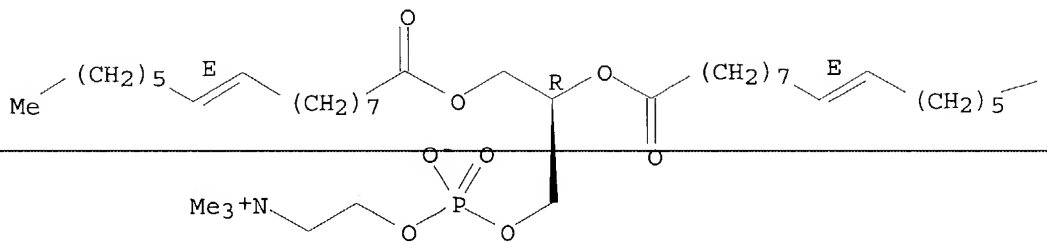
PAGE 1-B

Me

RN 56816-00-3 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9E)-1-oxo-9-hexadecenyl]oxy]-, inner salt, 4-oxide, (7R,18E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

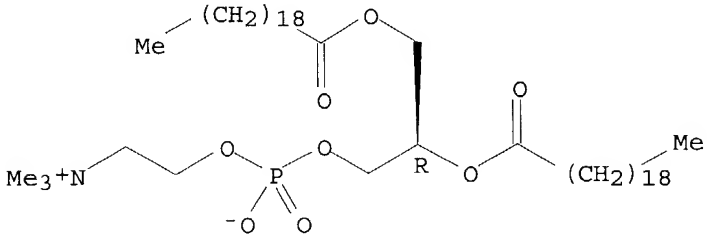
PAGE 1-A



PAGE 1-B

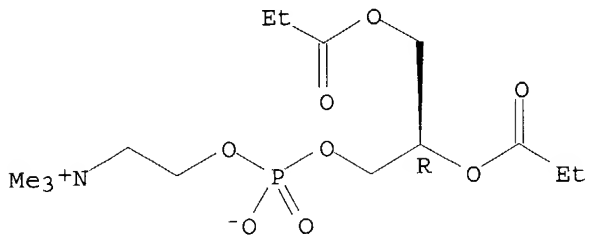
RN 61596-53-0 HCAPLUS
CN 3,5,9-Trioxa-4-phosphanonacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxoeicosyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



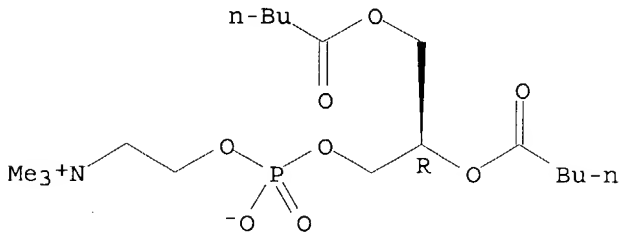
RN 66414-33-3 HCAPLUS
CN 3,5,9-Trioxa-4-phosphadodecan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-(1-oxopropoxy)-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



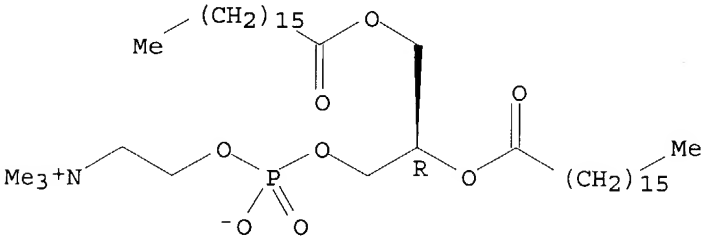
RN 66414-34-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatetradecan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxopentyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



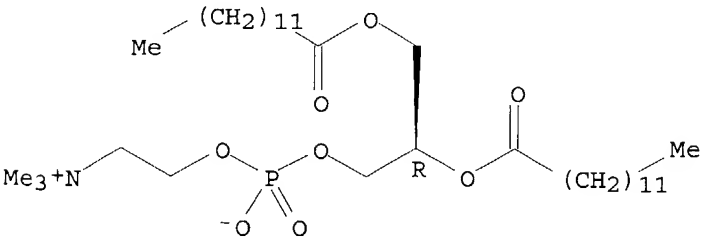
RN 70897-27-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphahexacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxoheptadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

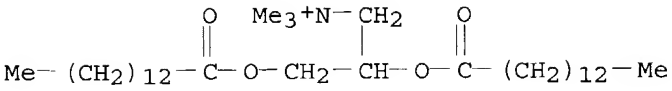


RN 71242-28-9 HCAPLUS
CN 3,5,9-Trioxa-4-phosphadocosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxotridecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

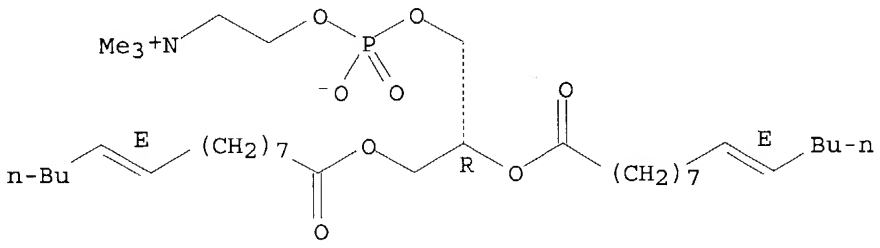


RN 72719-83-6 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(1-oxotetradecyl)oxy]- (9CI) (CA INDEX NAME)



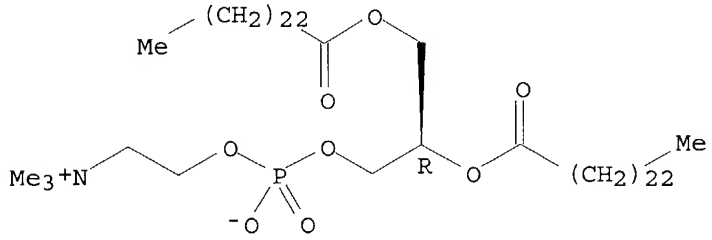
RN 76733-52-3 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatricos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9E)-1-oxo-9-tetradecenyl]oxy]-, inner salt, 4-oxide, (7R,18E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



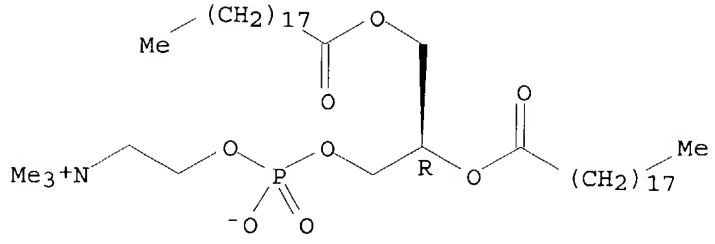
RN 91742-11-9 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatritriacontan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxotetracosyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



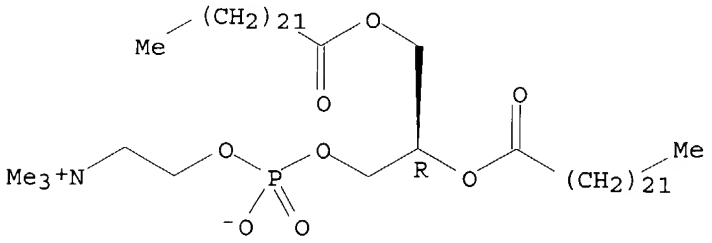
RN 95416-27-6 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaoctacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxononadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 112241-60-8 HCAPLUS
CN 3,5,9-Trioxa-4-phosphadotriacontan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxotricosyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

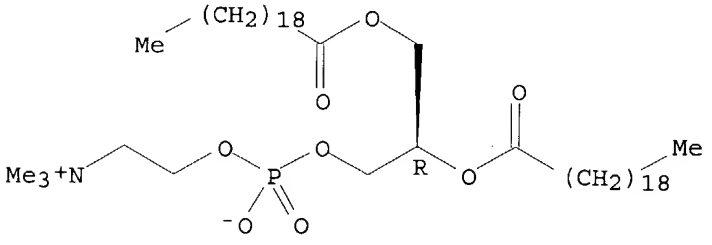


RN 137133-79-0 HCAPLUS
CN 3,5,9-Trioxa-4-phosphanonacosen-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(Z)-1-oxoeicosenyl]oxy]-, inner salt, 4-oxide, (7R,?Z)- (9CI) (CA INDEX NAME)

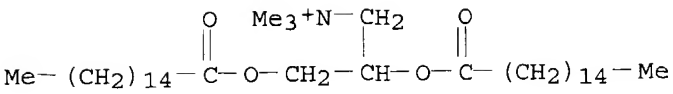
CM 1

CRN 61596-53-0
CMF C48 H96 N O8 P

Absolute stereochemistry.



RN 138915-91-0 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(1-oxohexadecyl)oxy]- (9CI) (CA INDEX NAME)



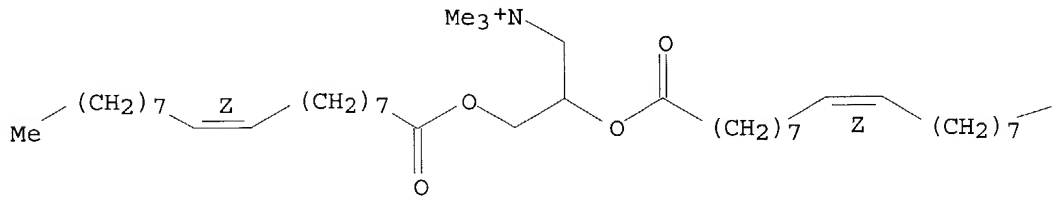
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

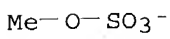
PAGE 1-A



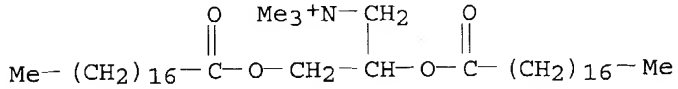
PAGE 1-B

CM 2

CRN 21228-90-0
CMF C H3 O4 S

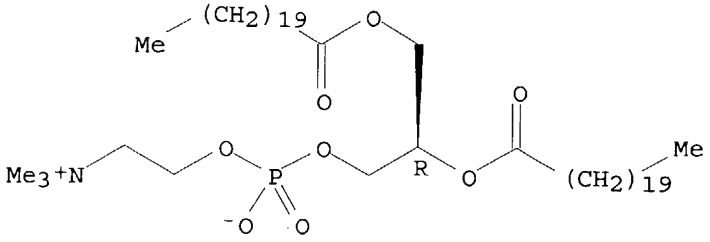


RN 173666-09-6 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)



RN 253685-28-8 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatriacontan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxoheneicosyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 41 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:753332 HCAPLUS
DOCUMENT NUMBER: 132:9620
TITLE: Stable envelope proteins for retroviral, viral and liposome vectors and use in gene and drug therapy
INVENTOR(S): Albritton, Lorraine M.; Zavorotinskaya, Tatiana
PATENT ASSIGNEE(S): The University of Tennessee Research Corporation, USA
SOURCE: PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9960110	A2	19991125	WO 1999-US11155	19990520
WO 9960110	A3	20000413		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9940898	A1	19991206	AU 1999-40898	19990520
US 6448390	B1	20020910	US 1999-315127	19990520

PRIORITY APPLN. INFO.: US 1998-86149P P 19980520
WO 1999-US11155 W 19990520

AB This invention includes retrovirus envelope mutants into which heterologous peptide or glycopeptide sequences can be linked for expression and stable presentation on retroviral vectors. The envelope mutants are characterized by the ability to restore the target penetration capability that is lost or greatly diminished upon fusion of heterologous

sequences to the wild type envelope protein and the ability to increase the fusion envelope protein stability and decrease envelope shedding from virus particles. The envelope mutants are created by rotating residues in at least one of 7 motifs. The disclosed envelope proteins also can be used in liposome or pseudotype-virus compns. for delivery of agents including nucleic acid mols. Methods of preparing and utilizing these envelope mutants in gene therapy are also described.

IC ICM C12N015-00
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 10

IT Rhabdoviridae
Vaccinia virus
(vectors; stable envelope proteins for retroviral, viral and liposome vectors and use in gene and drug therapy)

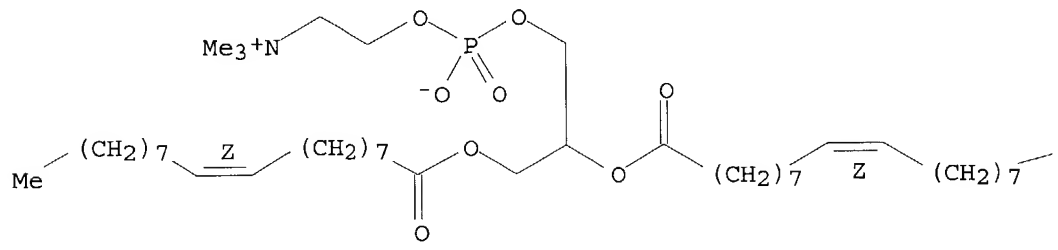
IT 4004-05-1, Dioleoylphosphatidylethanolamine 25322-68-3
68737-67-7, Dioleoylphosphatidylcholine **144189-73-1**,
DOTAP 151736-99-1 250695-61-5
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing; stable envelope proteins for retroviral, viral and liposome vectors and use in gene and drug therapy)

IT **68737-67-7**, Dioleoylphosphatidylcholine **144189-73-1**,
DOTAP
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing; stable envelope proteins for retroviral, viral and liposome vectors and use in gene and drug therapy)

RN 68737-67-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (18Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

RN 144189-73-1 HCAPLUS

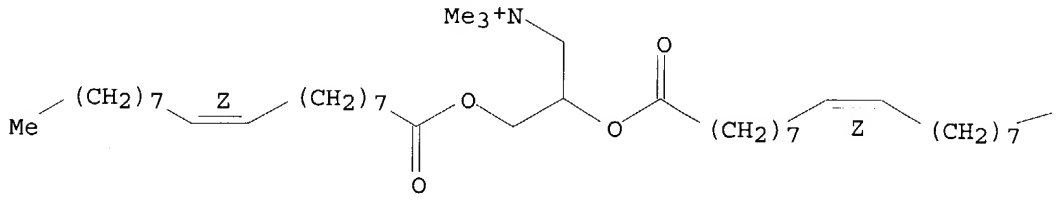
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO_3^-

L52 ANSWER 42 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:509584 HCAPLUS
DOCUMENT NUMBER: 131:262548
TITLE: Lamellarity of cationic liposomes and mode of preparation of lipoplexes affect transfection efficiency
AUTHOR(S): Zuidam, Nicolaas J.; Hirsch-Lerner, Danielle; Margulies, Sharon; Barenholz, Yechezkel
CORPORATE SOURCE: Department of Biochemistry, The Hebrew University-Hadassah Medical School, Jerusalem, 91120, Israel
SOURCE: Biochimica et Biophysica Acta (1999), 1419(2), 207-220
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Transfection of NIH-3T3 cells by a human growth hormone expression vector complexed with liposomes composed of N-(1-(2,3-dioleoyloxy)propyl)-N,N,N-trimethylammonium chloride (DOTAP) with or without helper lipids was studied. The transfection efficiency was dependent on the lamellarity of the liposomes used to prepare the lipoplexes. Multilamellar vesicles (MLV) were more effective than large unilamellar vesicles (LUV) of .apprx.100 nm, irresp. of lipid composition The optimal DNA/DOTAP mole ratio for transfection was ≤0.5, at which only 10-30% of DOTAP in the lipoplex is neutralized. Prolonged incubation time of lipoplexes before addition to cells slightly decreased the level of transfection. A major influence on the lipofection level was found when the mode of lipoplex preparation was varied. Mixing plasmid DNA and DOTAP/DOPE (1:1) LUV in two steps instead of one step resulted in a higher lipofection when at the first step the DNA/DOTAP mole ratio was 0.5 than when it was 2.0. Only static light-scattering measurement, which is related to particle size and particle size instability, revealed differences between the lipoplexes as a function of lamellarity of the vesicles (MLV or LUV), mixing order, and number of mixing steps. Other phys. properties of these lipoplexes were dependent only on the DNA/DOTAP mole ratio, i.e. the extent of DOTAP neutralization (as monitored by ionization of the fluorophore 4-heptadecyl-7-hydroxycoumarin) and the extent of defects in lipid organization (as monitored by level of exposure of the fluorophore 1-(4-trimethylammoniumphenyl)-6-phenyl-1,3,5-hexatriene to water). The secondary and tertiary structure of DNA in lipoplexes was evaluated by CD spectroscopy. The results of this study point out that the structure of lipoplexes should be physicochem. characterized at two different levels: the macro level, which relates to size and size instability, and the micro level, which relates to the properties described above which are involved in the intimate interaction between the plasmid DNA and the lipids. At the micro level, all parameters are reversible, history-independent and are determined by DNA/DOTAP mole ratio. On the other hand, the macro level (which is the most important for transfection efficiency) is history-dependent and not reversible.

CC 63-5 (Pharmaceuticals)

IT **DNA**
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lamellarity of cationic liposomes and mode of preparation of lipoplexes affect transfection efficiency)

IT **Drug delivery systems**
(liposomes; lamellarity of cationic liposomes and mode of preparation of lipoplexes affect transfection efficiency)

IT 4004-05-1, Dope **4235-95-4**, Dopc **144189-73-1**, Dotap
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lamellarity of cationic liposomes and mode of preparation of lipoplexes affect transfection efficiency)

IT **4235-95-4**, Dopc **144189-73-1**, Dotap
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lamellarity of cationic liposomes and mode of preparation of lipoplexes affect transfection efficiency)

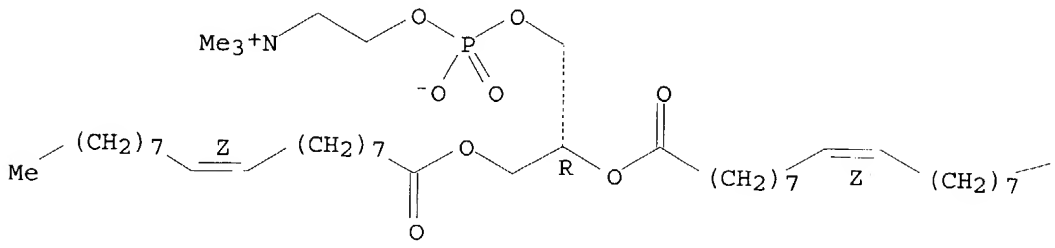
RN 4235-95-4 HCAPLUS

CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

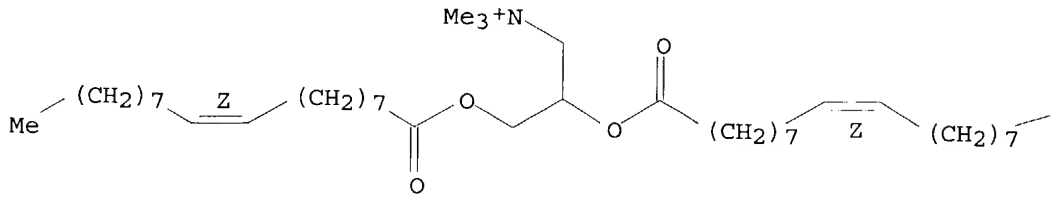
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO_3^-

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 43 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:219995 HCAPLUS
DOCUMENT NUMBER: 130:306599
TITLE: Antisense oligonucleotides capable of binding to multiple targets and their use in the treatment of respiratory disease
INVENTOR(S): Nyce, Jonathan W.
PATENT ASSIGNEE(S): East Carolina University, USA
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9913886	A1	19990325	WO 1998-US19419	19980917
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003087845	A1	20030508	US 1998-93972	19980609
CA 2304312	AA	19990325	CA 1998-2304312	19980917
AU 9893951	A1	19990405	AU 1998-93951	19980917
AU 752531	B2	20020919		
EP 1019065	A1	20000719	EP 1998-947089	19980917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9812650	A	20000822	BR 1998-12650	19980917
JP 2003517428	T2	20030527	JP 2000-511506	19980917

PRIORITY APPLN. INFO.:
US 1997-59160P P 19970917
US 1998-93972 A 19980609
WO 1998-US19419 W 19980917

AB Antisense oligonucleotides carrying sequences that will allow them to bind to more than one mRNA in a target cell are described. Such oligonucleotides can be used as a single treatment for diseases having more than one contributing pathway. In particular, oligonucleotides effective against genes involved in the etiol. of respiratory disease are targeted. Preferably, the oligonucleotides are low in adenosine (≤15%) and may have adenosines substituted with analogs. These

oligonucleotides are targeted to high (G+C) sequences within mRNAs. Thus, phosphorothioate antisense oligonucleotide (HAdA1AS, 5'-gatggagggcggcatggcggg-3') designed for the adenosine A1 receptor is provided. HAdA1AS significantly and specifically reduces the in vivo response to adenosine challenge in a dose-dependent manner, is effective in protection against aeroallergen-induced bronchoconstriction (house dust mite), has an unexpected long-term duration of effect (8.3 days for both PC50 adenosine and resistance), and is free of side effects that might be toxic to the recipient. Such oligonucleotides may be used for treating a disease or condition associated with lung airway, such as bronchoconstriction, inflammation, or allergies.

IC ICM A61K031-70
ICS A61K048-00; C07H021-00; C07H021-04; C12N005-10

CC 1-9 (Pharmacology)
Section cross-reference(s): 3

IT **Antisense oligonucleotides**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MTAs (multiple target antisense); antisense oligonucleotides capable of binding to multiple targets and their use in treatment of respiratory disease)

IT Allergy inhibitors
Anti-inflammatory agents
Antiasthmatics
Drug delivery systems
Surfactants
(antisense oligonucleotides capable of binding to multiple targets and their use in treatment of respiratory disease)

IT 5-HT receptors
Adenosine receptors
Adrenoceptors
Androgen receptors
Bradykinin receptors
CD34 (antigen)
Cell adhesion molecules
Chemokine receptors
Chemokines
Cholinergic receptors
Cyclophilins
Dopamine receptors
Enzymes, biological studies
Estrogen receptors
Fibronectins
GABA receptors
Glucagon receptors
Growth factors, animal
Histamine receptors
Immunoglobulin receptors
Immunoglobulins
Insulin receptors
Interleukin 1
Interleukin 1 receptors
Interleukin 11
Interleukin 1β
Interleukin 3
Interleukin 3 receptors
Interleukin 4
Interleukin 5
Interleukin 5 receptors

Interleukin 6
Interleukin 6 receptors
Interleukin 8
Interleukin 8 receptors
Interleukin 9
Interleukin receptors
Interleukins
LFA-1 (antigen)
Macrophage inflammatory protein 1α
Monocyte chemoattractant protein-1
Muscarinic receptors
Neuropeptide receptors
Neuropeptides
Neurotransmitters
Progesterone receptors
Prostanoid receptors
RANTES (chemokine)
Tachykinin receptors
Thyroid hormone receptors
Transcription factors
Transforming proteins
Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antisense oligonucleotides capable of binding to multiple targets and their use in treatment of respiratory disease)

IT **Drug delivery systems**
(capsules; antisense oligonucleotides capable of binding to multiple targets and their use in treatment of respiratory disease)

IT **Drug delivery systems**
(sprays; antisense oligonucleotides capable of binding to multiple targets and their use in treatment of respiratory disease)

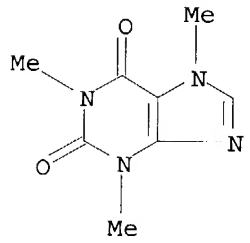
IT **58-08-2D**, Caffeine, oligonucleotides containing **58-55-9D**, Theophylline, oligonucleotides containing 62-49-7, Choline 63-38-7D, CDP, compds. with diacylglycerols **69-89-6D**, Xanthine, oligonucleotides containing 107-73-3, Choline phosphate 110-85-0D, Piperazine, oligonucleotides containing, biological studies 479-18-5D, Dyphylline, oligonucleotides containing 519-37-9D, Etophylline, oligonucleotides containing 652-37-9D, Acephylline, oligonucleotides containing
890-38-0D, 2'-Deoxyinosine, oligonucleotides containing 987-78-0, CDP-choline 2016-63-9D, Bamifylline, oligonucleotides containing 4546-68-3D, 2'-Deoxynebularine, oligonucleotides containing 5930-94-9D, 3-Nitropyrrole, oligonucleotides containing 6146-52-7D, 5-Nitroindole, oligonucleotides containing 9002-92-0 9002-93-1, Triton X-100 25322-68-3 25322-69-4 26336-38-9D, Poly(vinylamine), dextran and/or alkanoyl side chains 41078-02-8D, Enprofylline, oligonucleotides containing 60254-48-0D, oligonucleotides containing 95233-18-4, Atovaquone **99732-49-7**, Exosurf 106392-12-5, Ethylene oxide-propylene oxide block copolymer 108778-82-1, Survanta 126128-35-6D, oligonucleotides containing **144189-73-1** 191421-10-0D, oligonucleotides containing 222300-73-4 222300-75-6 222300-76-7 222300-77-8 222300-78-9 222300-79-0 222300-80-3 222300-81-4 222300-82-5 222300-83-6 222300-84-7 222300-85-8 222300-86-9 222300-87-0 222300-88-1 222300-89-2 222300-90-5 222300-91-6 222300-94-9 222300-98-3 222301-05-5 222301-06-6 222301-07-7 222301-10-2 222301-11-3 222301-12-4 222301-12-4 222301-15-7 222301-16-8 222301-17-9 222301-18-0 222301-19-1 222301-20-4 222301-21-5 222301-22-6 222301-23-7 222301-24-8 222301-25-9 222301-26-0 222301-27-1 222301-28-2

222301-31-7 222301-32-8 222301-34-0 222301-35-1 222301-36-2
222301-37-3 222301-38-4 222301-39-5 222301-40-8 222301-41-9
222301-42-0 222301-43-1 222301-44-2 222301-45-3 222301-46-4
222301-47-5 222301-48-6 222301-49-7 222301-50-0 222301-52-2
222301-53-3 222301-54-4 222301-55-5 222301-56-6 222301-57-7
222301-58-8 222301-59-9 222301-62-4 222301-63-5 222301-64-6
222301-65-7 222301-66-8 222301-67-9 222301-69-1 222301-73-7
222301-74-8 222301-75-9 222301-76-0 222301-77-1 222301-78-2
222301-79-3 222301-80-6 222301-81-7 222301-82-8 222301-83-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antisense oligonucleotides capable of binding to multiple targets and their use in treatment of respiratory disease)

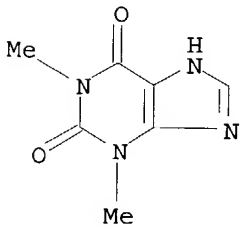
IT 53-43-0, Dehydroepiandrosterone 56-81-5, 1,2,3-Propanetriol, biological studies 57-03-4, Glycerol-3-phosphate 57-04-5, Dihydroxyacetone phosphate 96-26-4, Dihydroxyacetone 563-24-6, Glycerol 3-phosphatidylcholine **2644-64-6**, Dipalmitoylphosphatidylcholine 11029-02-0D, Dolichol, compds. 17364-18-0, Palmitoyl-Lysophosphatidylcholine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surfactant; antisense oligonucleotides capable of binding to multiple targets and their use in treatment of respiratory disease)

IT **58-08-2D**, Caffeine, oligonucleotides containing **58-55-9D**, Theophylline, oligonucleotides containing **69-89-6D**, Xanthine, oligonucleotides containing **99732-49-7**, Exosurf **144189-73-1**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antisense oligonucleotides capable of binding to multiple targets and their use in treatment of respiratory disease)

RN 58-08-2 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

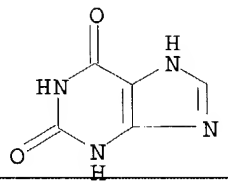


RN 58-55-9 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 69-89-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro- (9CI) (CA INDEX NAME)



RN 99732-49-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide, (7R)-, mixt. with formaldehyde polymer with oxirane and 4-(1,1,3,3-tetramethylbutyl)phenol and 1-hexadecanol (9CI) (CA INDEX NAME)

CM 1

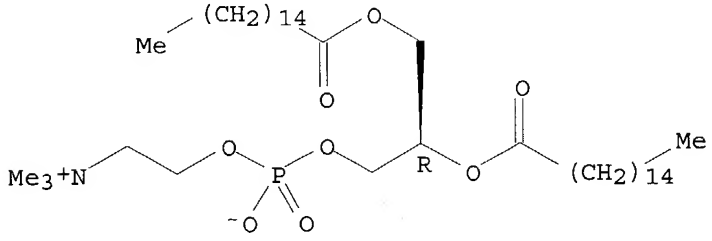
CRN 36653-82-4
CMF C16 H34 O

HO— $(CH_2)_{15}$ —Me

CM 2

CRN 63-89-8
CMF C40 H80 N O8 P

Absolute stereochemistry. Rotation (+).



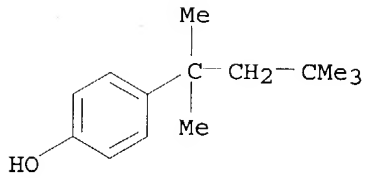
CM 3

CRN 25301-02-4
CMF (C14 H22 O . C2 H4 O . C H2 O)x
CCI PMS

CM 4

CRN 140-66-9

CMF C14 H22 O

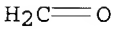


CM 5

CRN 75-21-8
CMF C2 H4 O

CM 6

CRN 50-00-0
CMF C H2 O



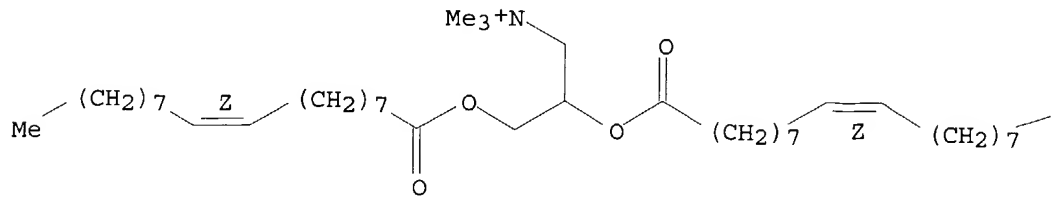
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



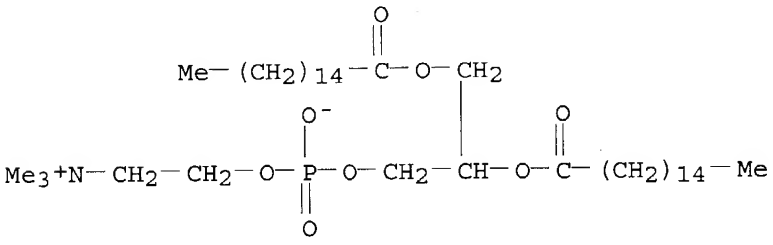
Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO_3^-

IT **2644-64-6**, Dipalmitoylphosphatidylcholine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surfactant; antisense oligonucleotides capable of binding to multiple targets and their use in treatment of respiratory disease)
RN 2644-64-6 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 44 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:621076 HCAPLUS
DOCUMENT NUMBER: 129:265462
TITLE: Dry powder formulations of polynucleotide complexes for inhalation delivery to the respiratory tract
INVENTOR(S): Szoka, Francis C., Jr.; Rolland, Alain; Wang, Jinkang
PATENT ASSIGNEE(S): Regents of the University of California, USA
SOURCE: U.S., 31 pp., Cont.-in-part of U.S. Ser. No. 482,110.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

US 5811406	A	19980922	US 1995-482254	19950609
US 5972600	A	19991026	US 1995-482110	19950607
CA 2224156	AA	19961227	CA 1996-2224156	19960528
WO 9641873	A1	19961227	WO 1996-US7867	19960528
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
AU 9659382	A1	19970109	AU 1996-59382	19960528
AU 708179	B2	19990729		
EP 836645	A1	19980422	EP 1996-916715	19960528
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11507922	T2	19990713	JP 1997-503085	19960528
AU 9921179	A1	19990513	AU 1999-21179	19990315
AU 720187	B2	20000525		

PRIORITY APPLN. INFO.:

US 1995-482110	A2	19950607
US 1995-485430	A2	19950607
US 1992-864876	B2	19920403
US 1992-913669	B2	19920714
US 1993-92200	B2	19930714
US 1995-482254	A	19950609
AU 1996-59381	A3	19960528
WO 1996-US7867	W	19960528

AB Polynucleotide complexes are stabilized by adding a cryoprotectant compound and lyophilizing the resulting formulation. The lyophilized formulations are milled or sieved into a dry powder formulation which may be used to deliver the polynucleotide complex. Delivery of the polynucleotide to a desired cell tissue is accomplished by contacting the tissue with the powder to rehydrate it. In a preferred embodiment, a dry powder formulation is used to transfer genetic information to the cells of the respiratory tract.

IC ICM A61K048-00

NCL 514044000

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 3

IT **Polynucleotides**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(complexes; dry powder formulations of polynucleotide complexes for inhalation delivery to the respiratory tract)

IT **Plasmids**
(lipid complexes; dry powder formulations of polynucleotide complexes for inhalation delivery to the respiratory tract)

IT **Drug delivery systems**
(powders, inhalants; dry powder formulations of polynucleotide complexes for inhalation delivery to the respiratory tract)

IT 57-09-0D, Ctab, polynucleotide complexes 57-88-5D, Cholesterol, polynucleotide complexes 124-03-8D, Cetyldimethylethylammonium bromide, polynucleotide complexes 2390-68-3D, Ddab, polynucleotide complexes 2462-63-7D, Dope, polynucleotide complexes **4235-95-4D**, Dopc, polynucleotide complexes 25496-72-4D, Monooleoylglycerol, polynucleotide complexes **104162-48-3D**, Dotma, polynucleotide complexes 124050-78-8D, polynucleotide complexes **144189-73-1D**, Dotap, polynucleotide complexes **153312-64-2D**, Dmrie, polynucleotide complexes **168479-03-6D**, Dospa, polynucleotide complexes

186584-03-2D, Agmatinyl carboxycholesterol acetic acid salt, polynucleotide complexes 186584-05-4D, polynucleotide complexes 186584-07-6D, polynucleotide complexes 186584-09-8D, polynucleotide complexes 186584-14-5D, polynucleotide complexes 186584-17-8D, polynucleotide complexes 186589-60-6D, JK 154, polynucleotide complexes 186743-48-6D, polynucleotide complexes 213478-72-9D, polynucleotide complexes 213478-73-0D, polynucleotide complexes 213478-74-1D, polynucleotide complexes 213478-75-2D, polynucleotide complexes 213478-76-3D, polynucleotide complexes 213478-77-4D, polynucleotide complexes

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(dry powder formulations of polynucleotide complexes for inhalation delivery to the respiratory tract)

IT **4235-95-4D**, Dopc, polynucleotide complexes **104162-48-3D**, Dotma, polynucleotide complexes **144189-73-1D**, Dotap, polynucleotide complexes **153312-64-2D**, Dmrie, polynucleotide complexes **168479-03-6D**, Dospa, polynucleotide complexes

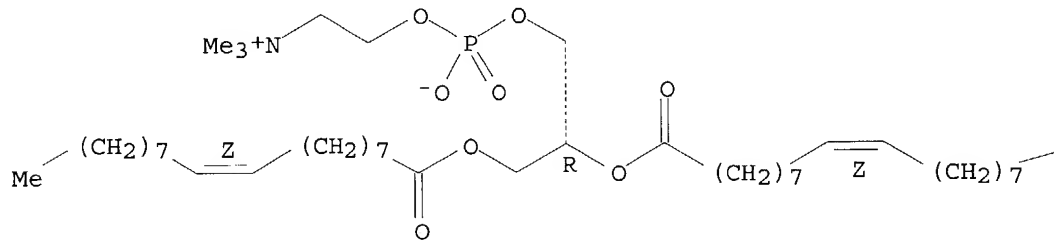
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(dry powder formulations of polynucleotide complexes for inhalation delivery to the respiratory tract)

RN 4235-95-4 HCAPLUS

CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



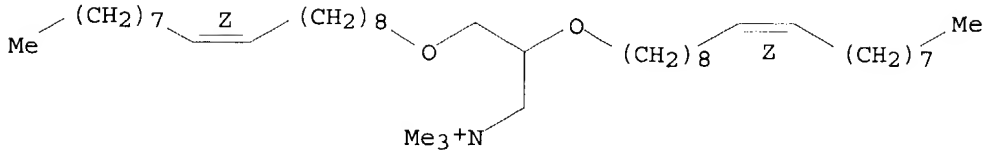
PAGE 1-B

Me

RN 104162-48-3 HCAPLUS

CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



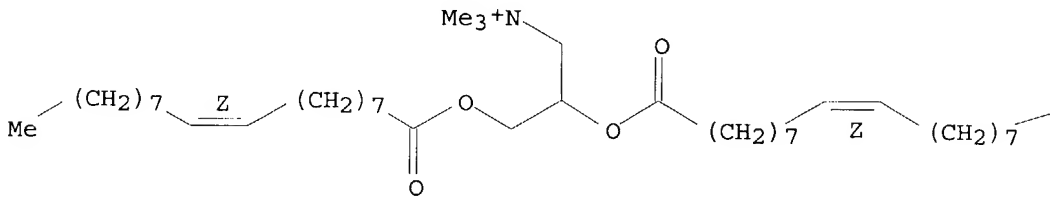
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

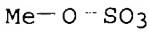
PAGE 1-A



PAGE 1-B

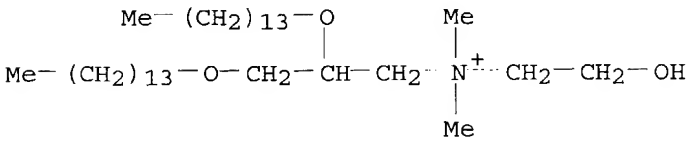
CM 2

CRN 21228-90-0
CMF C H3 O4 S



RN 153312-64-2 HCAPLUS

CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



● Br^-

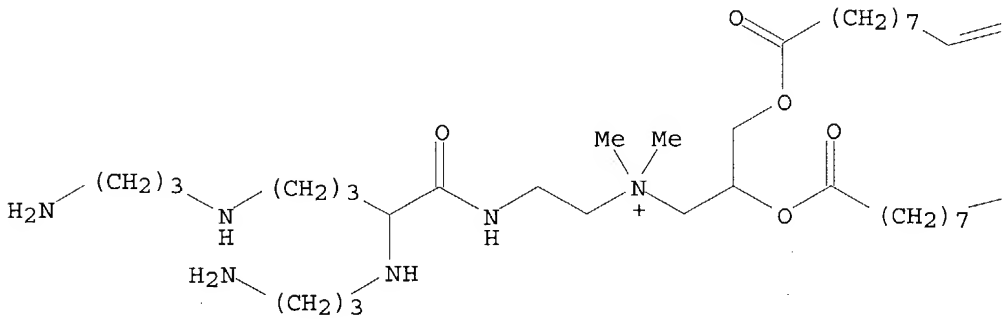
RN 168479-03-6 HCAPLUS
CN 1-Propanaminium, N-[2-[[2,5-bis[(3-aminopropyl)amino]-1-oxopentyl]amino]ethyl]-N,N-dimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, salt with trifluoroacetic acid (1:1) (9CI) (CA INDEX NAME)

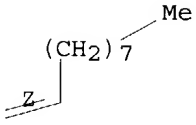
CM 1

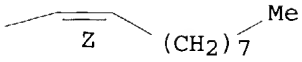
CRN 168479-02-5
CMF C54 H107 N6 O5

Double bond geometry as shown.

PAGE 1-A

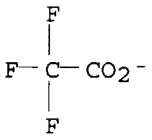






CM 2

CRN 14477-72-6
CMF C2 F3 O2



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 45 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:484928 HCAPLUS
DOCUMENT NUMBER: 129:113548
TITLE: Pharmaceutical or cosmetic compositions containing homogeneously charged particulate vector
INVENTOR(S): Betbeder, Didier; Major, Michel
PATENT ASSIGNEE(S): Biovector Therapeutics S.A., Fr.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9829102	A1	19980709	WO 1997-FR2397	19971223

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

FR 2757768	A1	19980703	FR 1996-16146	19961227
FR 2757768	B1	19990402		
AU 9856688	A1	19980731	AU 1998-56688	19971223
EP 946153	A1	19991006	EP 1997-952990	19971223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001508425	T2	20010626	JP 1998-529682	19971223

PRIORITY APPLN. INFO.: FR 1996-16146 A 19961227
WO 1997-FR2397 W 19971223

AB The invention concerns a particulate carrier comprising a non-liquid hydrophilic nucleus; an amphiphilic lamella characterized in that the nucleus carries a global cationic, anionic or neutral charge and that the amphiphilic lamella carries a global charge of same polarity as that carried by the nucleus. The invention also concerns a pharmaceutical or cosmetic composition or a nutrient additive containing such a vector. Thus, maltodextrin (500 g) was treated with 7 g NaBH4 followed by the reaction with NaOH, 30.25 mL epichlorohydrin and 382.3 g glycidyltrimethylammonium chloride. The resulting gel was diluted with water a and neutralized with HOAc. Nanoparticle carriers were prepared by using the above polysaccharide and a phospholipid.

IC ICM A61K009-51
ICS A61K009-127

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 17, 33, 62

IT **Drug delivery systems**
(liposomes; pharmaceutical or cosmetic compns. containing homogeneously charged particulate vector)

IT **Drug delivery systems**
(nanoparticles; pharmaceutical or cosmetic compns. containing homogeneously charged particulate vector)

IT Analgesics
Anesthetics
Anti-inflammatory agents
Antiasthmatics
Antibacterial agents
Antibiotics
Anticonvulsants
Antidepressants
Antidiabetic agents
Antihistamines
Antimalarials
Antipsychotics
Antitumor agents
Antiviral agents
Anxiolytics
Appetite depressants
Cardiovascular agents
Cosmetics
Fungicides
Hemostatics
Hypnotics and Sedatives
Immunomodulators
Insecticides
Muscarinic antagonists
Surfactants
Vaccines
(pharmaceutical or cosmetic compns. containing homogeneously charged particulate vector)

IT **Antigens**

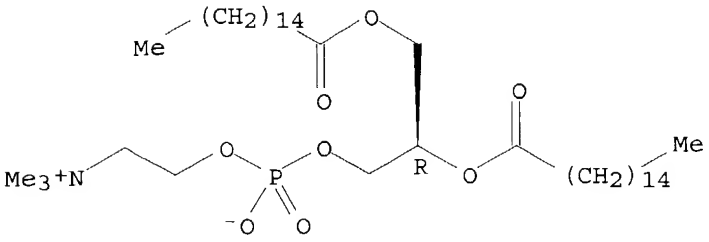
Ceramides
Fatty acids, biological studies
Glycerides, biological studies
Glycolipids
Hormones, animal, biological studies
Lipids, biological studies
Lipopolysaccharides
Lipoproteins
Nucleic acids
Nucleosides, biological studies
Nucleotides, biological studies
Oligomers
Oligosaccharides, biological studies
Peptides, biological studies
Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphatidylglycerols
Phosphatidylserines
Phospholipids, biological studies
Polymers, biological studies
Polysaccharides, biological studies
Porphyrins
Proteins, general, biological studies
Proteoglycans, biological studies
Steroids, biological studies
Vitamins
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical or cosmetic compns. containing homogeneously charged particulate vector)

IT 57-88-5, Cholesterol, biological studies **63-89-8**, DPPC 124-30-1, Stearylamine 3036-82-6, Dipalmitoylphosphatidylserine 4537-77-3, Dipalmitoylphosphatidylglycerol 4537-78-4, Distearoylphosphatidylglycerol 9004-34-6, Cellulose, biological studies 9004-54-0, Dextran, biological studies 9005-25-8, Starch, biological studies 9050-36-6D, Maltodextrin, ethers 19698-29-4, Dipalmitoylphosphatidic acid 30170-00-4, Dimyristoylphosphatidic acid 61361-72-6, Dimyristoylphosphatidylglycerol 62700-69-0, Dioleoylphosphatidylglycerol 137720-22-0D, 1-acylated **144189-73-1**, DOTAP
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical or cosmetic compns. containing homogeneously charged particulate vector)

IT **63-89-8**, DPPC **144189-73-1**, DOTAP
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical or cosmetic compns. containing homogeneously charged particulate vector)

RN 63-89-8 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



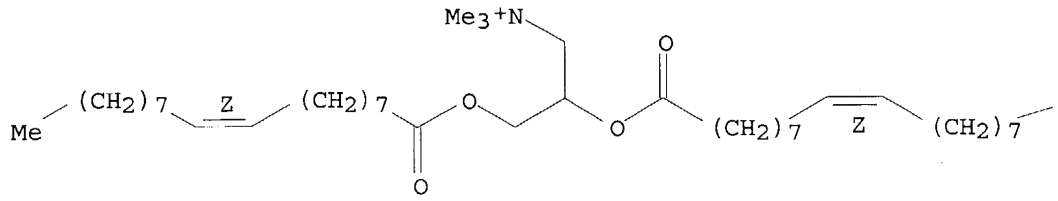
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me— O— SO_3^-

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 46 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:378050 HCAPLUS
DOCUMENT NUMBER: 129:99906
TITLE: Lipid- and adenoviral-mediated gene transfer into AIDS-Kaposi's sarcoma cell lines
AUTHOR(S): Campain, Julie A.; Matassa, Angela A.; Felgner, Philip L.; Barnhart, Kerry M.; Curiel, David T.; Harrison, Gail S.
CORPORATE SOURCE: University of Colorado Health Sciences Center, Denver, CO, 80262, USA
SOURCE: Cancer Gene Therapy (1998), 5(3), 131-143
CODEN: CGTHEG; ISSN: 0929-1903
PUBLISHER: Appleton & Lange
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Kaposi's sarcoma (KS) is the most frequent malignancy occurring in HIV-pos. individuals. AIDS-KS is a more aggressive disease than the classical form, frequently having a rapid clin. course with numerous serious complications. Current systemic treatments for KS, such as chemotherapy and the administration of biol. modifiers, are complicated by both the drug resistance of the tumor and the dose-limiting toxicity of the reagents. The relative accessibility of many KS lesions makes the disease a particularly attractive candidate for in vivo gene therapy protocols. In this regard, we are interested in delivering conditionally toxic suicide and/or antiangiogenic vectors to accomplish targeted cell death selectively in AIDS-KS cells. To this end, we examined both cationic lipid- and adenoviral-mediated DNA transfection methods. Using the firefly luciferase reporter gene, we optimized numerous variables known to be important in lipid-mediated DNA transfection, including lipid formulation, the amount of lipid and DNA, lipid/DNA ratio, and cell concentration

Under optimal transfection conditions, .apprx.5-25% of KS cells expressed the introduced DNA sequences. Adenoviral-mediated DNA delivery was more efficient than lipid delivery in 4 of 5 primary KS cell lines. Two of the lines (RW248 and RW376) were transduced by adenovirus at frequencies approaching 100%; two cell lines (CVU-1 and RW80) gave efficiencies of 20-35%. Two immortalized KS cell lines (KS Y-1 and KS SLK) were poorly infected, giving a transduction efficiency of <5%. These findings demonstrate that gene transfer into AIDS-KS cells is feasible, and suggest that vector strategies may be permissive for translating gene therapy approaches for the disease.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 3

IT **DNA**
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid- and adenoviral-mediated gene transfer into AIDS-Kaposi's sarcoma cell lines)

IT **Drug delivery systems**
(liposomes, cationic; lipid- and adenoviral-mediated gene transfer into AIDS-Kaposi's sarcoma cell lines)

IT **68737-67-7**, Dioleoylphosphatidylcholine **153312-64-2**, DMRIE **158571-62-1**, Lipofectamine **182919-20-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid- and adenoviral-mediated gene transfer into AIDS-Kaposi's sarcoma cell lines)

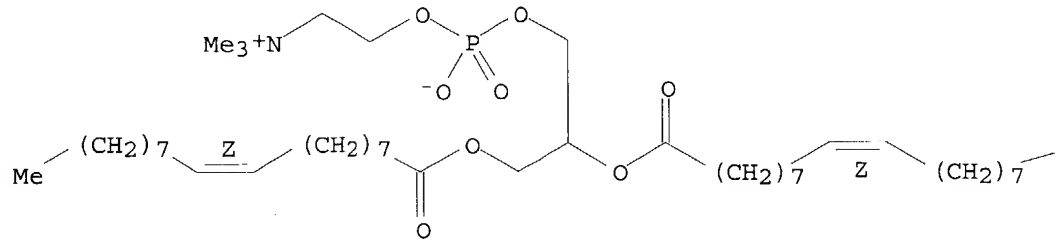
IT **68737-67-7**, Dioleoylphosphatidylcholine **153312-64-2**, DMRIE **158571-62-1**, Lipofectamine **182919-20-6**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid- and adenoviral-mediated gene transfer into AIDS-Kaposi's sarcoma cell lines)

RN 68737-67-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (18Z)-(9CI) (CA INDEX NAME)

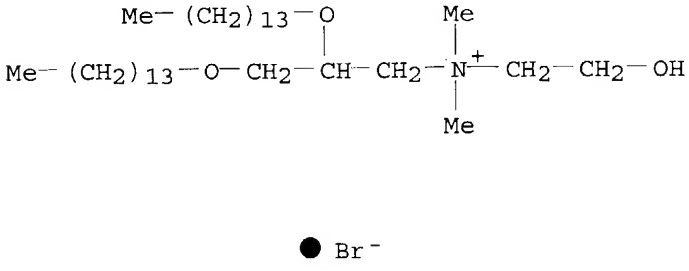
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

RN 153312-64-2 HCAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



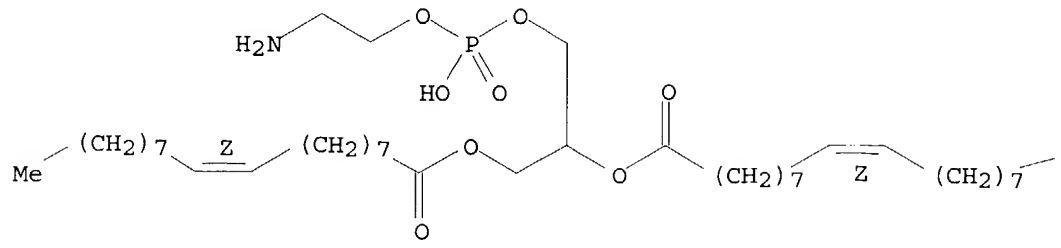
RN 158571-62-1 HCAPLUS
CN 1-Propanaminium, N-[3-[[3-[[4-[(3-aminopropyl)amino]butyl]amino]propyl]amino]-3-oxopropyl]-N,N-dimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, salt with trifluoroacetic acid (1:1), mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

CM 2

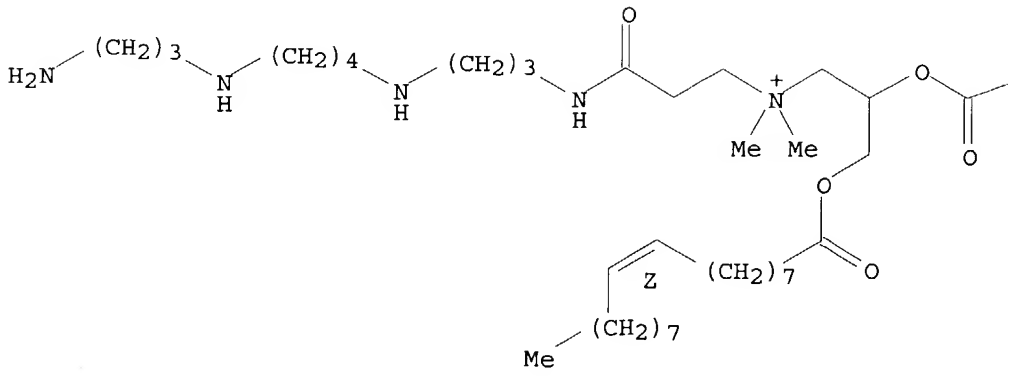
CRN 185097-43-2
CMF C54 H106 N5 O5 . C2 F3 O2

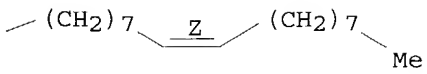
CM 3

CRN 181508-68-9
CMF C54 H106 N5 O5

Double bond geometry as shown.

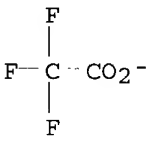
PAGE 1-A



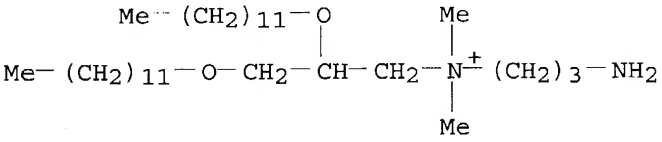


CM 4

CRN 14477-72-6
CMF C2 F3 O2



RN 182919-20-6 HCAPLUS
CN 1-Propanaminium, N-(3-aminopropyl)-2,3-bis(dodecyloxy)-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

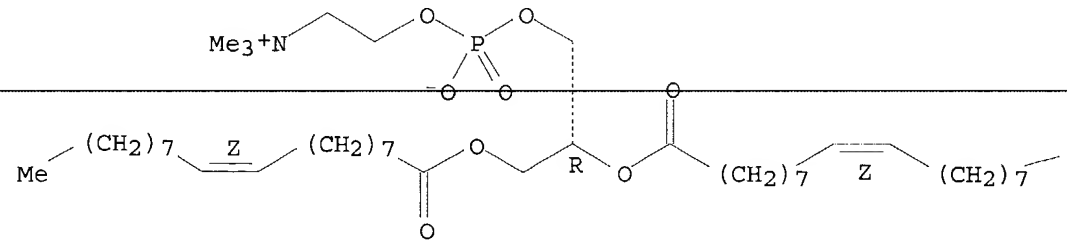
L52 ANSWER 47 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:229461 HCAPLUS
DOCUMENT NUMBER: 129:19588
TITLE: Structural requirements for cationic lipid mediated phosphorothioate oligonucleotides delivery to cells in culture
AUTHOR(S): Bennett, C. F.; Mirejovsky, D.; Crooke, R. M.; Tsai, Y. J.; Felgner, J.; Sridhar, C. N.; Wheeler, C. J.; Felgner, P. L.
CORPORATE SOURCE: ISIS Pharmaceuticals, Carlsbad, CA, 92008, USA
SOURCE: Journal of Drug Targeting (1998), 5(3), 149-162
CODEN: JDTAEH; ISSN: 1061-186X
PUBLISHER: Harwood Academic Publishers

DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of 2,3-dialkyloxypropyl quaternary ammonium lipids containing hydroxyalkyl chains on the quaternary amine were synthesized, formulated with dioleoylphosphatidylethanolamine (DOPE) and assayed for their ability to enhance the activity of an intercellular adhesion mol. 1 (ICAM-1) antisense oligonucleotide, ISIS 1570. Cationic liposomes prepared with hydroxyethyl, hydroxypropyl, and hydroxybutyl substituted cationic lipid all enhanced the activity of the ICAM-1 antisense oligonucleotide. Cationic lipids containing hydroxypentyl quaternary amines only marginally enhanced the activity of ISIS 1570. Hydroxyethyl cationic lipids synthesized with dimyristyl (C14:0) and dioleyl (C18:1) alkyl chains were equally effective. Activity of cationic lipids containing saturated alkyl groups decreased as the chain length increased, i.e. the dimyristyl (C14:0) was more effective than dipalmityl (C16:0) lipid, which was more effective than distearyl (C18:0). The phase transition temperature of cationic lipids containing saturated aliphatic chains was 56 for the distearyl lipid, 42 for the dipalmityl lipid, and 24° for the dimyristyl lipid. Cationic lipids with dioleyl alkyl chains required DOPE for activity, with optimal activity occurring at 50 mol%. In contrast, a dimyristyl containing cationic lipid did not require DOPE to enhance the activity of ISIS 1570. Formulation with different phosphatidylethanolamine derivs., revealed that optimal activity was obtained with DOPE. These studies demonstrate that several cationic lipid species enhance the activity of phosphorothioate antisense oligonucleotides and provide further information on the mechanism by which cationic lipids enhance the activity of phosphorothioate oligodeoxynucleotides.
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1
IT **Drug delivery systems**
(liposomes; structural requirements for cationic liposome mediated phosphorothioate oligonucleotides delivery to cells)
IT **Antisense oligonucleotides**
Phosphatidylethanolamines, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(structural requirements for cationic liposome mediated phosphorothioate oligonucleotides delivery to cells)
IT 2462-63-7, DOPE **4235-95-4**, DOPC 20255-95-2, Dimyristoylphosphatidylethanolamine **104162-48-3**, DOTMA **109908-95-4** **119113-07-4** **153312-64-2**, DMRIE **153985-22-9**, DORIE **165467-64-1**, DORI **207602-65-1** **207602-66-2** **207602-67-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(structural requirements for cationic liposome mediated phosphorothioate oligonucleotides delivery to cells)
IT **4235-95-4**, DOPC **104162-48-3**, DOTMA **109908-95-4** **119113-07-4** **153312-64-2**, DMRIE **153985-22-9**, DORIE **165467-64-1**, DORI **207602-65-1** **207602-66-2** **207602-67-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(structural requirements for cationic liposome mediated phosphorothioate oligonucleotides delivery to cells)
RN 4235-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

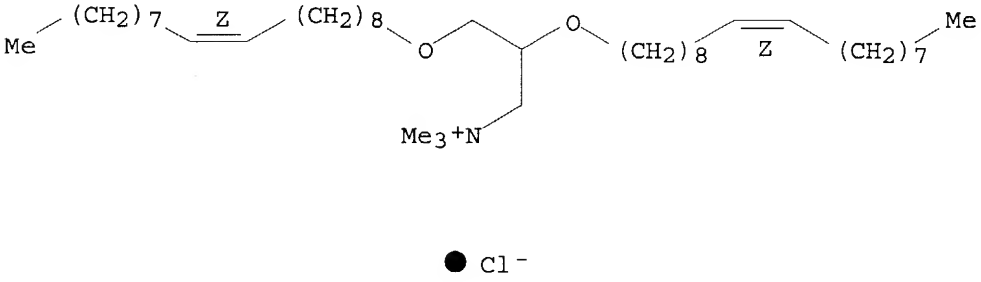
PAGE 1-A



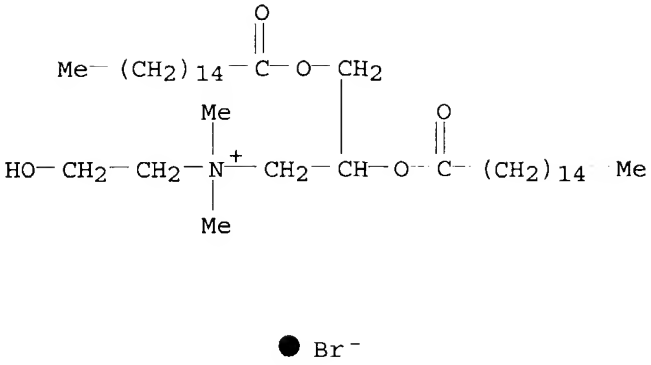
PAGE 1-B

RN 104162-48-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

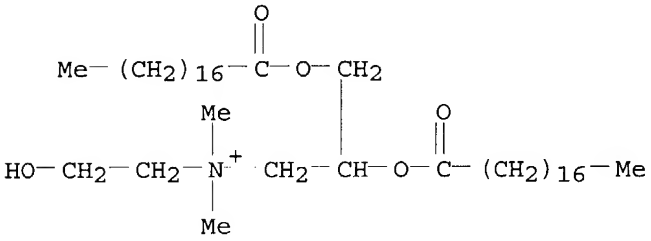


RN 109908-95-4 HCAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis[(1-oxohexadecyl)oxy]-, bromide (9CI) (CA INDEX NAME)



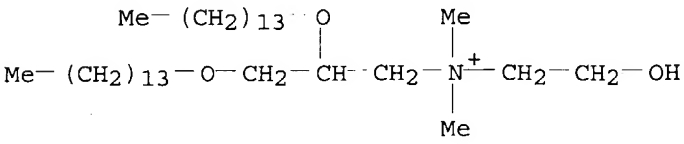
● Br^-

RN 119113-07-4 HCAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis[(1-oxooctadecyl)oxy]-, bromide (9CI) (CA INDEX NAME)



● Br^-

RN 153312-64-2 HCAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)

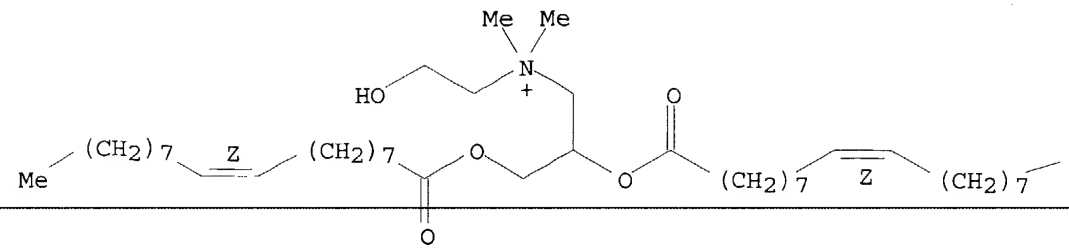


● Br^-

RN 153985-22-9 HCAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



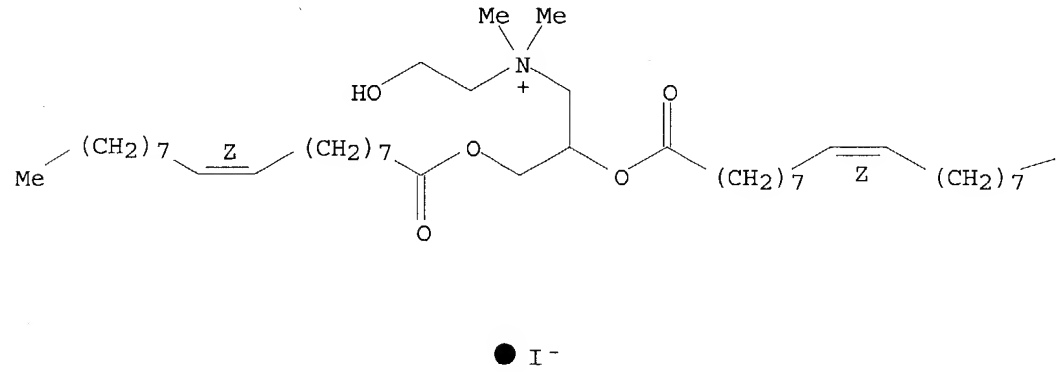
PAGE 1-B

Me

RN 165467-64-1 HCAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, iodide (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



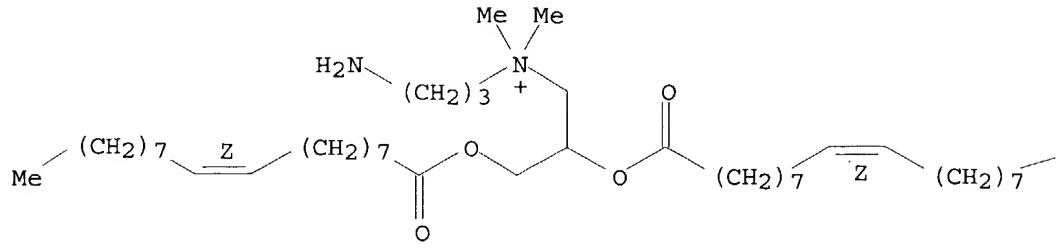
PAGE 1-B

Me

RN 207602-65-1 HCAPLUS
CN 1-Propanaminium, N-(3-aminopropyl)-N,N-dimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, bromide (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



● Br^-

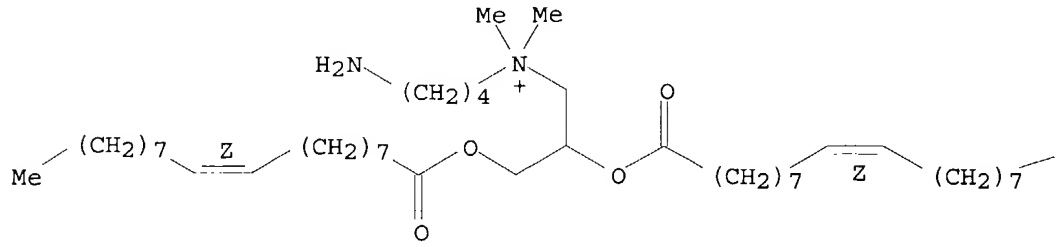
PAGE 1-B

Me

RN 207602-66-2 HCAPLUS
CN 1-Butanaminium, 4-amino-N-[2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]propyl]-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



● Br^-

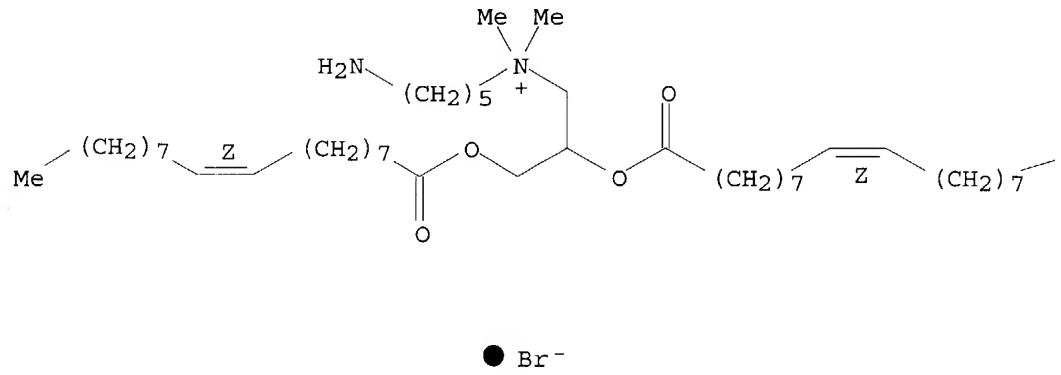
PAGE 1-B

Me

RN 207602-67-3 HCAPLUS
CN 1-Pentanaminium, 5-amino-N-[2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]propyl]-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

L52 ANSWER 48 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:207280 HCAPLUS
DOCUMENT NUMBER: 128:275101
TITLE: Gas and gaseous precursor filled microspheres as topical and subcutaneous delivery vehicles
INVENTOR(S): Unger, Evan C.; Matsunaga, Terry O.; Yellowhair, David
PATENT ASSIGNEE(S): Imarx Pharmaceutical Corp., USA
SOURCE: U.S., 40 pp., Cont.-in-part of U.S. Ser. No. 307,305.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5733572	A	19980331	US 1994-346426	19941129
US 5088499	A	19920218	US 1990-569828	19900820
WO 9109629	A1	19910711	WO 1990-US7500	19901219
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AT 180170	E	19990615	AT 1991-902857	19901219
ES 2131051	T3	19990716	ES 1991-902857	19901219
JP 3309356	B2	20020729	JP 1991-503276	19901219
JP 05502675	T2	19930513		
US 5228446	A	19930720	US 1991-717084	19910618
WO 9222247	A1	19921223	WO 1992-US2615	19920331
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AU 9220020	A1	19930112	AU 1992-20020	19920331
AU 667471	B2	19960328		
JP 06508364	T2	19940922	JP 1993-500847	19920331
JP 3456584	B2	20031014		
EP 616508	A1	19940928	EP 1992-912456	19920331
EP 616508	B1	20010718		
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AT 203148	E	20010815	AT 1992-912456	19920331
ES 2159280	T3	20011001	ES 1992-912456	19920331
US 5469854	A	19951128	US 1993-76239	19930611
US 5580575	A	19961203	US 1993-76250	19930611
US 5348016	A	19940920	US 1993-88268	19930707
US 5542935	A	19960806	US 1993-160232	19931130
US 5585112	A	19961217	US 1993-159687	19931130
US 5769080	A	19980623	US 1994-199462	19940222
WO 9428874	A1	19941222	WO 1994-US5633	19940519
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US 5773024	A	19980630	US 1994-307305	19940916
CA 2177713	AA	19950608	CA 1994-2177713	19941130
WO 9515118	A1	19950608	WO 1994-US13817	19941130
W: AU, CA, CN, JP				
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EP 740528	A1	19961106	EP 1995-908414	19941130
EP 740528	B1	20030326		
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JP 09506098	T2	19970617	JP 1995-515763	19941130
AT 235228	E	20030415	AT 1995-908414	19941130
US 5571497	A	19961105	US 1995-468056	19950606
CN 1180310	A	19980429	CN 1996-193069	19960327
CN 1102045	B	20030226		
US 6001335	A	19991214	US 1996-665719	19960618
US 5935553	A	19990810	US 1996-758179	19961125
US 6743779	B1	20040601	US 1997-841169	19970429
US 5985246	A	19991116	US 1997-888426	19970708
AU 9856271	A1	19980507	AU 1998-56271	19980224
AU 713127	B2	19991125		
AU 9888405	A1	19981203	AU 1998-88405	19981012
AU 731072	B2	20010322		
HK 1013625	A1	20000420	HK 1998-114978	19981223
AU 9910043	A1	19990304	AU 1999-10043	19990104

GR 3036877	T3	20020131	GR 2001-401740		20011011
PRIORITY APPLN. INFO.:			US 1989-455707	B2	19891222
			US 1990-569828	A2	19900820
			US 1991-716899	B2	19910618
			US 1991-717084	A2	19910618
			US 1993-76239	A2	19930611
			US 1993-76250	A2	19930611
			US 1993-159674	B2	19931130
			US 1993-159687	A2	19931130
			US 1993-160232	A2	19931130
			US 1994-307305	A2	19940916
			WO 1990-US7500	W	19901219
			US 1991-716793	A	19910618
			US 1991-750877	A3	19910826
			US 1992-818069	A3	19920108
			WO 1992-US2615	A	19920331
			US 1992-967974	A3	19921027
			US 1993-17683	A3	19930212
			US 1993-18112	B3	19930217
			US 1993-85608	A3	19930630
			US 1993-88268	A3	19930707
			US 1993-163039	A3	19931206
			US 1994-212553	B2	19940311
			AU 1994-70416	A3	19940519
			US 1994-346426	A	19941129
			AU 1995-21850	A3	19941130
			WO 1994-US13817	W	19941130
			US 1995-395683	A3	19950228
			US 1995-468056	A3	19950606
			US 1995-471250	A3	19950606
			US 1996-640554	B2	19960501
			US 1996-665719	A3	19960618
			US 1997-785661	B2	19970117

AB Gas and gaseous precursor filled microspheres, and foams provide novel topical and s.c. delivery vehicles for various active ingredients, including drugs and cosmetics. Gas and gaseous precursor filled microcapsules were prepared from dipalmitoylphosphatidylcholine.

IC ICM A61K009-127
NCL 424450000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 62
IT Acacia
Alcohols, biological studies
Alkanes, biological studies
Allergy inhibitors
Amines, biological studies
Anthocyanins
Anti-inflammatory agents
Antibacterial agents
Antibiotics
Anticoagulants
Antioxidants
Antisense oligonucleotides
Antiviral agents
Bentonite, biological studies
Buffers
Canola oil
Carbohydrates, biological studies
Cardiovascular agents

Chelating agents
Collagens, biological studies
Coloring materials
Corn oil
Cosmetics
DNA
Diuretics
Dystrophin
Elastins
Enkephalins
Enzymes, biological studies
Essential oils
Esters, biological studies
Fatty acids, biological studies
Fluoropolymers, biological studies
Foaming agents
Fungicides
Gases
Gene, animal
Glycolipids
Glycols, biological studies
Growth factors, animal
Hormones, animal, biological studies
Immunosuppressants
Lipids, biological studies
Micelles
Olive oil
Peanut oil
Peptides, biological studies
Perfluorocarbons
Petrolatum
Phosphatidic acids
Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphatidylglycerols
Phosphatidylinositols
Phosphatidylserines
Phospholipids, biological studies
Polyamides, biological studies
Polyesters, biological studies
Polyolefins
Polyoxyalkylenes, biological studies
Polysaccharides, biological studies
Polyurethanes, biological studies
Preservatives
Protozoacides
Quaternary ammonium compounds, biological studies
Radionuclides, biological studies
Safflower oil
Sphingolipids
Sulfatides
Sulfoxides
Terpenes, biological studies
Tocopherols
Tuberculostatics
Vitamins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gas and gaseous precursor filled microspheres as topical and s.c. delivery vehicles)

IT **Drug delivery systems**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcapsules; gas and gaseous precursor filled microspheres as topical and s.c. delivery vehicles)

IT **Drug delivery systems**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ointments; gas and gaseous precursor filled microspheres as topical and s.c. delivery vehicles)

IT 50-02-2, Dexamethasone 50-03-3, Hydrocortisone acetate 50-04-4, Cortisone acetate 50-23-7, Hydrocortisone 50-24-8 50-33-9, Phenylbutazone, biological studies 50-56-6, Oxytocin, biological studies 50-70-4, Sorbitol, biological studies 50-78-2, Aspirin 50-81-7, Ascorbic acid, biological studies 51-05-8, Procaine hydrochloride 51-34-3, Scopolamine 52-21-1 52-67-5, Penicillamine 53-03-2, Prednisone 53-36-1, Methylprednisolone acetate 53-86-1, Indomethacin 54-05-7, Chloroquine 54-11-5, Nicotine 54-85-3, Isoniazid 56-75-7, Chloramphenicol 56-81-5, 1,2,3-Propanetriol, biological studies 57-09-0, Cetyltrimethylammonium bromide 57-11-4, Octadecanoic acid, biological studies 57-13-6, Urea, biological studies 57-15-8, Chlorobutanol 57-55-6, 1,2-Propanediol, biological studies 57-88-5, Cholesterol, biological studies **58-08-2**, Caffeine, biological studies 59-02-9, α-Tocopherol 60-00-4, Edta, biological studies 60-54-8, Tetracycline 61-32-5, Methicillin 61-33-6, Penicillin g, biological studies 61-68-7, Mefenamic acid 64-17-5, Ethanol, biological studies 65-49-6, p-Aminosalicylic acid 65-85-0, Benzoic acid, biological studies 66-79-5, Oxacillin 67-43-6, DTPA 67-56-1, Methanol, biological studies 67-68-5, Dmso, biological studies 67-78-7, Triamcinolone diacetate 68-19-9D, Cyanocobalamin, derivs. 68-41-7, Cycloserine 69-53-4, Ampicillin 69-72-7, Salicylic acid, biological studies 73-78-9, Lidocaine hydrochloride 74-88-4, Iodomethane, biological studies 74-98-6, Propane, biological studies 75-00-3, Chloroethane 75-10-5, Difluoromethane 75-18-3, Methyl sulfide 75-19-4, Cyclopropane 75-28-5, Isobutane 75-29-6, 2-Chloropropane 75-31-0, 2-Aminopropane, biological studies 75-34-3, 1,1-Dichloroethane 75-43-4, Dichlorofluoromethane 75-45-6, Chlorodifluoromethane 75-46-7, Trifluoromethane 75-56-9, biological studies 75-61-6, Dibromodifluoromethane 75-63-8, Bromotrifluoromethane 75-69-4, Trichlorofluoromethane 75-71-8, Dichlorodifluoromethane 75-72-9, Chlorotrifluoromethane 75-73-0, Tetrafluoromethane 76-13-1, 1,1,2-Trichloro-1,2,2-trifluoroethane 76-15-3, 1-Chloro-1,1,2,2,2-pentafluoroethane 76-16-4, Hexafluoroethane 76-19-7, Perfluoropropane 76-25-5, Triamcinolone acetonide 77-92-9, Citric acid, biological studies 78-78-4, 2-Methylbutane 78-79-5, biological studies 78-80-8 79-81-2, Retinol palmitate 80-08-0 83-43-2, Methylprednisolone 87-08-1, Penicillin v 87-73-0, Saccharic acid 93-60-7, Methyl nicotinate 94-14-4, Isobutyl p-aminobenzoate 94-26-8, Butylparaben 95-80-7, 2,4-Diaminotoluene 96-40-2, 3-Chlorocyclopentene 96-49-1, 1,3-Dioxolan-2-one 98-96-4, Pyrazinamide 99-76-3, Methylparaben 100-51-6, Benzyl alcohol, biological studies 102-71-6, biological studies 103-41-3, Benzyl cinnamate 106-98-9, 1-Butene, biological studies 106-99-0, 1,3-Butadiene, biological studies 107-00-6, 1-Butyne 107-01-7, 2-Butene 107-25-5, Methyl vinyl ether 107-41-5, Hexylene glycol 108-95-2, Phenol, biological studies 109-66-0, n-Pentane, biological studies 109-67-1, 1-Pentene 109-92-2, Ethyl vinyl ether 109-93-3 110-27-0, Isopropyl myristate 110-44-1, Sorbic acid 111-02-4, Squalene 111-42-2, biological studies 112-30-1, 1-Decanol 112-53-8, 1-Dodecanol 112-72-1, Myristyl alcohol 112-80-1, 9-Octadecenoic acid (Z)-, biological studies 112-92-5, n-Octadecyl alcohol 114-07-8, Erythromycin 115-10-6, Methyl ether 115-25-3,

Octafluorocyclobutane 118-42-3, Hydroxychloroquine 118-58-1, Benzyl salicylate 121-54-0, Benzethonium chloride 122-18-9, Benzyldimethyl hexadecylammonium chloride 122-57-6, 4-Phenyl-3-butene-2-one 123-03-5 124-03-8, Cetyldimethylethylammonium bromide 124-38-9, Carbon dioxide, biological studies 124-40-3, Dimethylamine, biological studies 124-94-7, Triamcinolone 125-02-0, Prednisolone sodium phosphate 125-04-2, Hydrocortisone sodium succinate 126-07-8, Griseofulvin 126-18-1, Smilagenin 126-19-2, Sarsasapogenin 129-20-4, Oxyphenbutazone 130-95-0, Quinine 133-51-7, Meglumine antimonate 136-47-0, Tetracaine hydrochloride 137-66-6, Ascorbyl palmitate 139-07-1, Benzyldimethyldodecylammonium chloride 139-08-2, Benzyldimethyl tetradecylammonium chloride 140-72-7, Cetylpyridinium bromide 141-43-5, biological studies 143-28-2, Oleyl alcohol 143-62-4, Digitoxigenin 147-52-4, Nafcillin 151-21-3, Sodium lauryl sulfate, biological studies 151-73-5, Betamethasone sodium phosphate 154-21-2, Lincomycin 287-23-0, Cyclobutane 302-79-4, Retinoic acid 334-99-6, Nitrosotrifluoromethane 335-02-4, Nitrotrifluoromethane 335-05-7, Trifluoromethanesulfonyl fluoride 335-57-9, Perfluoroheptane 338-65-8, 2-Chloro-1,1-difluoroethane 350-51-6, 3-Fluorostyrene 353-36-6, Fluoroethane 353-85-5, Trifluoroacetonitrile 353-87-7, Bromodifluoronitrosomethane 354-25-6, 1-Chloro-1,1,2,2-tetrafluoroethane 354-72-3, Nitrosopentafluoroethane 354-80-3, Perfluoroethylamine 354-81-4, Nitropentafluoroethane 355-25-9, Decafluorobutane 355-42-0, Perfluorohexane 357-26-6, Perfluoro-1-butene 359-35-3, 1,1,2,2-Tetrafluoroethane 360-89-4, Perfluoro-2-butene 371-67-5, 1,1,1-Trifluorodiazoethane 371-77-7 371-78-8, Trifluoromethyl sulfide 373-52-4, Bromofluoromethane 374-07-2, 1,1-Dichloro-1,2,2,2-tetrafluoroethane 376-87-4, Perfluoropent-1-ene 378-44-9, Betamethasone 420-45-1, 2,2-Difluoropropane 420-46-2, 1,1,1-Trifluoroethane 421-56-7, Chlorodifluoronitromethane 421-83-0, Trifluoromethanesulfonyl chloride 423-26-7, Heptafluoro-1-nitrosopropane 423-33-6, Propane, 1,1,1,2,2,3,3,heptafluoro-3-nitro- 430-53-5, 1,1-Dichloro-2-fluoroethane 435-97-2, Phenprocoumon 443-48-1, Metronidazole 460-12-8, Butadiyne 460-13-9, 1-Fluoropropane 461-68-7, Tetrafluoroallene 463-49-0, Allene 463-58-1, Carbonyl sulfide 463-82-1, Neopentane 465-65-6, Naloxone 465-99-6, Hederagenin 482-54-2, Cyclohexanediaminetetraacetic acid 503-17-3, 2-Butyne 508-02-1, Oleanolic acid 508-99-6, Hydrocortisone cypionate 514-36-3, Fludrocortisone acetate 521-13-1, Cholesterol butyrate 526-95-4, Gluconic acid 532-32-1, Sodium benzoate 536-33-4, Ethionamide 540-54-5, 1-Chloropropane 547-64-8, Methyl lactate 555-43-1, Glycerol tristearate 555-44-2, Glycerol tripalmitate 555-45-3, Glycerol trimyristate 559-40-0, Octafluorocyclopentene 563-45-1, 3-Methyl-1-butene 563-46-2, 2-Methyl-1-butene 582-25-2, Potassium benzoate 590-19-2, 1,2-Butadiene 591-93-5, 1,4-Pentadiene 593-53-3, Fluoromethane 593-70-4, Chlorofluoromethane 593-98-6, Bromochlorofluoromethane 594-11-6, Methylcyclopropane 598-23-2, 3-Methyl-1-butyne 598-53-8, Methyl iso-propyl ether 598-56-1 598-61-8, Methylcyclobutane 601-34-3, Cholesterol palmitate 623-84-7, Propylene glycol diacetate 624-72-6, 1,2-Difluoroethane 624-91-9, Methyl nitrite 625-04-7, 4-Amino-4-methylpentan-2-one 632-58-6, Tetrachlorophthalic acid 644-62-2 661-54-1, 3,3,3-Trifluoropropyne 661-97-2, 1,1,1,2,3,3-Hexafluoro-2,3 dichloropropane 677-56-5, 1,1,1,2,2,3-Hexafluoropropane 678-26-2, Perfluoropentane 684-16-2, Hexafluoro acetone 685-63-2, Hexafluoro-1,3-butadiene 689-97-4, Vinyl acetylene 692-50-2, Perfluoro-2-butyne 697-11-0, Perfluorocyclobutene 767-00-0, 4-Cyanophenol 768-94-5, Amantadine 822-16-2, Sodium stearate 921-13-1, Chlorodinitromethane
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(gas and gaseous precursor filled microspheres as topical and s.c. delivery vehicles)

IT 927-84-4, Trifluoromethyl peroxide 928-45-0, Butyl nitrate 929-59-9 931-91-9, Hexafluorocyclopropane 987-24-6, Betamethasone acetate 1070-11-7, Ethambutol hydrochloride 1119-94-4, Lauryltrimethylammonium bromide 1119-97-7, Myristyltrimethylammonium bromide 1177-87-3, Dexamethasone acetate 1180-43-4, Cholesterol isobutyrate 1191-96-4, Ethylcyclopropane 1256-86-6, Cholesterol sulfate 1314-13-2, Zinc oxide, biological studies 1321-10-4, Chlorocresol 1323-39-3, Propylene glycol monostearate 1323-83-7, Glycerol distearate 1327-43-1, Magnesium aluminum silicate 1338-39-2, Sorbitan monolaurate 1338-41-6, Sorbitan monostearate 1338-43-8, Sorbitan monooleate 1344-95-2, Calcium silicate 1397-89-3, Amphotericin b 1398-61-4, Chitin 1400-61-9, Nystatin 1404-04-2, Neomycin 1405-37-4, Capreomycin sulfate 1406-16-2, Vitamin d 1406-18-4, Vitamin e 1493-03-4, Difluoroiodomethane 1597-82-6, Paramethasone acetate 1630-94-0, 1,1-Dimethylcyclopropane 1722-62-9, Mepivacaine hydrochloride 1759-88-2 1842-05-3, 1,1-Dichloro-1,2-difluoroethane 2022-85-7, Flucytosine 2314-97-8, Iodotrifluoromethane 2366-52-1, 1-Fluorobutane 2375-03-3, Methylprednisolone sodium succinate 2392-39-4, Dexamethasone sodium phosphate 2462-63-7, Dioleoylphosphatidylethanolamine 2511-95-7, 1,2-Dimethyl-cyclopropane 2551-62-4, Sulfur hexafluoride **2644-64-6**, Dipalmitoylphosphatidylcholine 2671-68-3, Lanosterol acetate 2809-21-4, Etidronic acid 3116-76-5, Dicloxacillin 3385-03-3, Flunisolide 3485-14-1, Cyclacillin 3511-16-8, Hetacillin 3529-04-2, Benzyldimethyl hexadecylammonium bromide 3810-74-0, Streptomycin sulfate 3858-89-7, Chloroprocaine hydrochloride 3992-98-1, Ergosterol palmitate **4539-70-2**, Distearoylphosphatidylcholine 4697-36-3, Carbenicillin 4786-20-3, Crotononitrile 4901-75-1, 3-Ethyl-3-methyldiaziridine 5534-09-8, Beclomethasone dipropionate 5536-17-4, Vidarabine 5611-51-8, Triamcinolone hexacetonide 5714-22-7, Sulfur fluoride (S2F10) 6000-74-4, Hydrocortisone sodium phosphate 6556-12-3, Glucuronic acid 7047-84-9, Aluminum monostearate 7235-40-7, Beta carotene 7281-04-1, Benzyldimethyldodecylammonium bromide 7440-01-9, Neon, biological studies 7440-15-5, Rhenium, biological studies 7440-24-6, Strontium, biological studies 7440-37-1, Argon, biological studies 7440-59-7, Helium, biological studies 7440-63-3, Xenon, biological studies 7440-65-5, Yttrium, biological studies 7553-56-2, Iodine, biological studies 7631-86-9, Silicon dioxide, biological studies 7637-07-2, Boron trifluoride, biological studies 7681-14-3, Prednisolone tebutate 7727-37-9, Nitrogen, biological studies 7732-18-5, Water, biological studies 7782-41-4, Fluorine, biological studies 7782-44-7, Oxygen, biological studies 7783-82-6, Tungsten hexafluoride 9000-07-1, Carrageenan 9000-30-0, Guar gum 9000-65-1, Tragacanth 9000-69-5, Pectin 9001-78-9, Alkaline phosphatase 9002-06-6, Thymidine kinase 9002-18-0, Agar 9002-60-2, Corticotropin, biological studies 9002-61-3, Human chorionic gonadotropin 9002-62-4, Prolactin, biological studies 9002-68-0, FSH 9002-71-5, Thyrotropin 9002-76-0, Gastrin 9002-84-0, Polytetrafluoroethylene 9002-86-2, Polyvinylchloride 9002-88-4, Polyethylene 9002-89-5, Polyvinyl alcohol 9003-07-0, Polypropylene 9003-39-8, Povidone 9003-53-6, Polystyrene 9004-10-8, Insulin, biological studies 9004-34-6, Cellulose, biological studies 9004-53-9, Dextrin 9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid 9004-62-0, Hydroxyethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methylcellulose 9004-67-5, Methylcellulose 9004-98-2, Polyoxyethylene oleyl ether 9004-99-3, Polyoxyethylene stearate 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9005-37-2, Propylene glycol alginate

9005-38-3, Sodium alginate 9005-49-6, Heparin, biological studies 9005-64-5, Polysorbate 20 9005-65-6, Polysorbate 80 9005-66-7, Polysorbate 40 9005-67-8, Polysorbate 60 9005-79-2, Glycogen, biological studies 9005-82-7, Amylose 9007-12-9, Calcitonin 9007-27-6, Chondroitin 9007-92-5, Glucagon, biological studies 9011-14-7, Polymethylmethacrylate 9011-97-6, Cholecystokinin 9012-36-6, Agarose 9012-72-0, Glucan 9013-95-0, Levan 9014-63-5, Xylan 9026-93-1, Adenosine deaminase 9034-40-6, Luteinizing hormone releasing hormone 9035-81-8, Trypsin inhibitor 9036-88-8, Mannan 9037-22-3, Amylopectin 9037-55-2, Galactan 9037-90-5, Fructan 9046-38-2, Galacturonan 9046-40-6, Pectic acid 9050-04-8 9057-02-7, Pullulan 9060-75-7, L-Arabinan 9072-19-9, Fucoidan 10024-97-2, Nitrous oxide, biological studies 10549-91-4 11103-57-4, Vitamin a 11138-66-2, Xanthan gum 12001-79-5, Vitamin k 13264-41-0, Cetyldimethylethylammonium chloride 13292-46-1, Rifampin 15686-71-2, Cephalexin 15687-27-1, Ibuprofen 17435-78-8, Cholesterol glucuronide 18010-40-7, Bupivacaine hydrochloride 18323-44-9, Clindamycin **18656-38-7**, Dimyristoylphosphatidylcholine **18656-40-1**, Dilauroylphosphatidylcholine 18773-88-1, Benzyldimethyl tetradecylammonium bromide 19247-09-7 19600-01-2, Ganglioside gm 2 20947-95-9 22204-53-1, Naproxen 22494-42-4, Diflunisal 22916-47-8, Miconazole 24521-77-5 24634-61-5, Potassium sorbate 24764-97-4, 2-Bromobutyraldehyde 24937-47-1, Polyarginine 25038-59-9, Pet, biological studies 25104-18-1, Polylysine 25212-18-4, Polyarginine 25322-68-3 25322-69-4, Polypropylene glycol 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid 26171-23-3, Tolmetin 26266-57-9, Sorbitan monopalmitate 26787-78-0, Amoxicillin 27070-61-7, Hexafluoropropane 29593-08-6 30516-87-1, Azidothymidine 31362-50-2, Bombesin 31566-31-1, Glyceryl monostearate 33735-55-6 34077-87-7, Dichlorotrifluoroethane 34787-01-4, Ticarcillin 35602-69-8, Cholesterol stearate 36322-90-4, Piroxicam 36637-19-1, Etidocaine hydrochloride 36653-82-4, Cetyl alcohol 36791-04-5, Ribavirin 37266-93-6, Sucrose laurate 37318-31-3, Sucrose stearate 37330-34-0 37331-28-5, Pustulan 37377-93-8, β-Lipotropin 37758-47-7, Ganglioside gm1 38000-06-5, Polylysine 38194-50-2, Sulindac 38821-53-3, Cephradine 39300-95-3, Sucrose palmitate 39422-22-5, γ-Lipotropin 50370-12-2, Cefadroxil 50402-72-7, 2,3,6-Trimethylpiperidine 50972-17-3, Bacampicillin 53563-63-6, Glycerol dimyristate 53994-73-3, Cefaclor 57223-18-4, 1-Nonen-3-yne 57916-92-4, Carbomer 934p 59227-89-3, Azone 59277-89-3, Acyclovir 60095-23-0 60495-58-1, Galactocarolose 64612-25-5, Fucan 65277-42-1, Ketoconazole 67382-96-1, Melanin concentrating hormone **67896-63-3**, Dipentadecanoylphosphatidylcholine 68302-57-8, Amlexanox 68354-92-7 68354-99-4 **68737-67-7**, Dioleoylphosphatidylcholine 69992-87-6, Keratan 73294-85-6 75634-40-1, Dermatan 76822-97-4 79217-60-0, Cyclosporin 98023-09-7 106392-12-5, Poloxamer 108173-78-0 109144-61-8 **113669-21-9** 116632-15-6, 1,2,3-Nonadecane-tricarboxylic acid-2-hydroxytrimethylester 117076-33-2 118248-91-2 127512-30-5, Cholesteryl(4'-trimethylammonio)butanoate

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gas and gaseous precursor filled microspheres as topical and s.c. delivery vehicles)

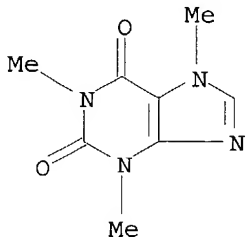
IT **132172-61-3** 161293-59-0 161441-83-4 172261-50-6 172261-51-7 172261-52-8 172261-53-9 172261-54-0 172261-55-1 172261-56-2 172261-57-3 172261-58-4 173855-10-2 186198-32-3 205645-72-3

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gas and gaseous precursor filled microspheres as topical and s.c.

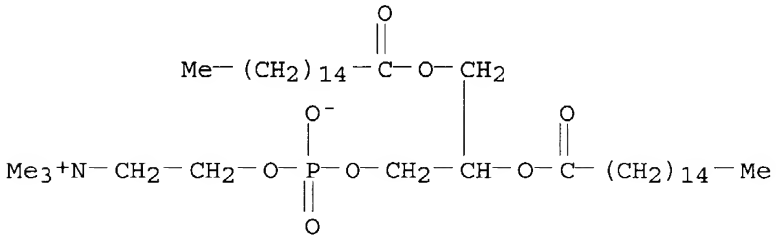
delivery vehicles)

IT **58-08-2**, Caffeine, biological studies **2644-64-6**,
Dipalmitoylphosphatidylcholine **4539-70-2**,
Distearoylphosphatidylcholine **18656-38-7**,
Dimyristoylphosphatidylcholine **18656-40-1**,
Dilauroylphosphatidylcholine **67896-63-3**,
Dipentadecanoylphosphatidylcholine **68737-67-7**,
Dioleoylphosphatidylcholine **113669-21-9 132172-61-3**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gas and gaseous precursor filled microspheres as topical and s.c. delivery vehicles)

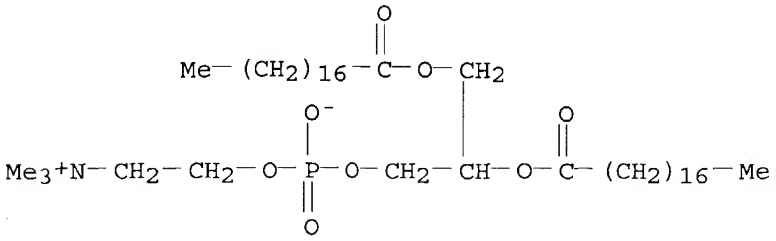
RN 58-08-2 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



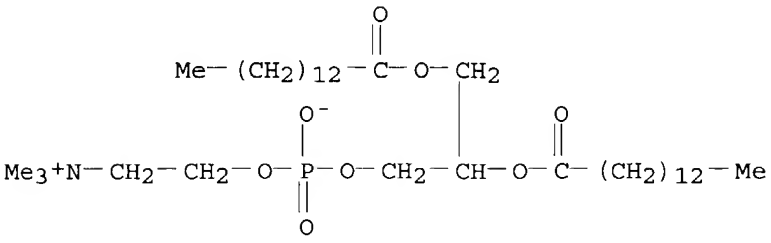
RN 2644-64-6 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



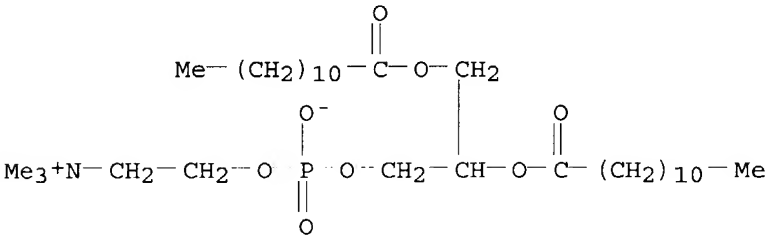
RN 4539-70-2 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



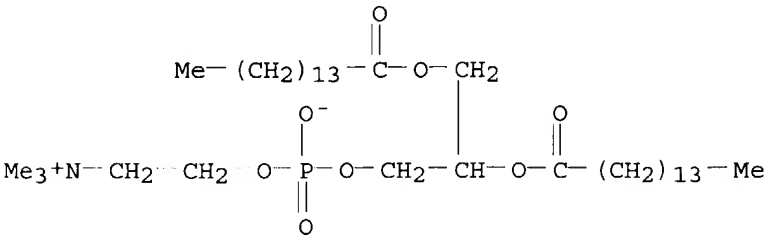
RN 18656-38-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatricosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxotetradecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 18656-40-1 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheneicosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxododecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



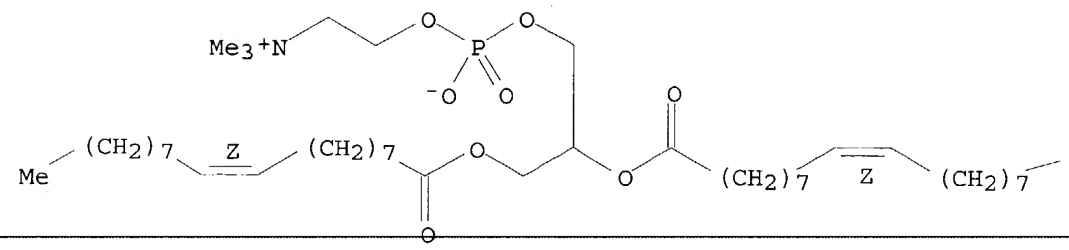
RN 67896-63-3 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatetracosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxopentadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 68737-67-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (18Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



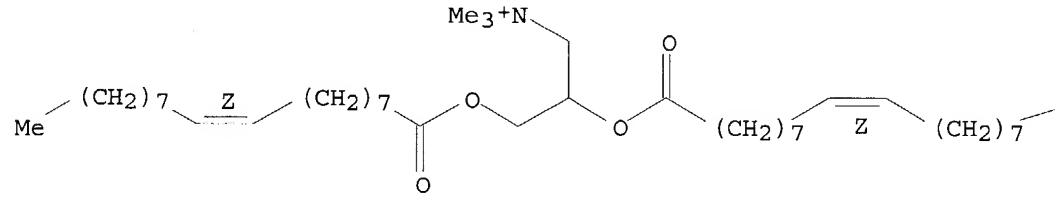
PAGE 1-B

Me

RN 113669-21-9 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



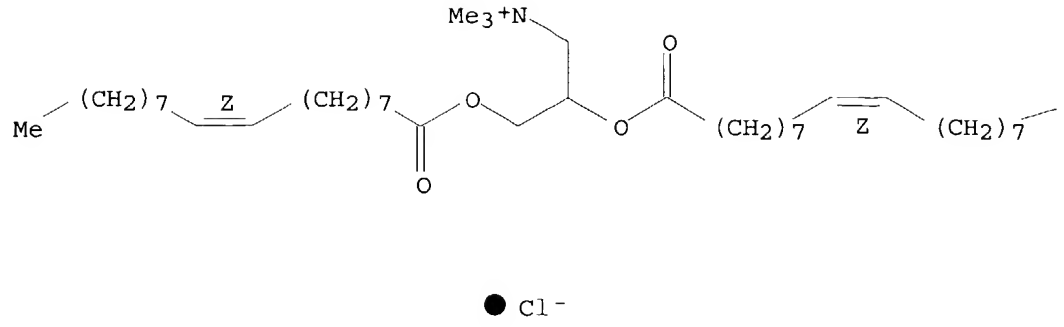
PAGE 1-B

Me

RN 132172-61-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-,
chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

REFERENCE COUNT: 314 THERE ARE 314 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 49 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:203965 HCAPLUS
DOCUMENT NUMBER: 129:153139
TITLE: Major limitations in the use of cationic liposomes for DNA delivery
AUTHOR(S): Filion, Mario C.; Phillips, Nigel C.
CORPORATE SOURCE: Facultede Pharmacie, Univ. de Montreal, Montreal, QC, H3C 3J7, Can.
SOURCE: International Journal of Pharmaceutics (1998), 162(1-2), 159-170
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Liposomal vectors formulated with cationic lipids and then fusogenic phospholipid dioleyolphosphatidylethanolamine (DOPE) are usually used to target DNA inside mammalian cells. Since macrophages constitute the major site of liposome localization after parenteral administration we felt it prudent to examine the effect of cationic liposomes on the production of several important immuno-inflammatory modulators secreted by activated macrophages. In addition, we have evaluated the toxicity of different cationic liposome formulations towards phagocytic macrophages and non-phagocytic T-lymphocytes. Our results indicate that cationic liposomes are able to down-regulate the synthesis of the protein kinase C (PKC)-dependent mediators nitric oxide (NO), tumor necrosis factor-α (TNF-α) and prostaglandin E2 (PGE2) by activated macrophages after in vitro incubation under non-toxic conditions or after in vivo treatment, while the production of PKC-independent IL-6 is not modified. We have shown that cationic lipids possess potent anti-inflammatory activity in vivo.

Prolonged incubation (>3 h) of macrophages with cationic liposomes induced a high level of toxicity (ED50<50 nmol/mL) that was not seen with non-phagocytic T-cells (ED50>1000 nmol/mL). The rank order of toxicity was DOPE/dimethyldioctadecylammonium bromide (DDAB)>DOPE/dioleoyltrimethyl ammoniumpropane (DOTAP)=DOPE/dimethylaminoethanecarbamoyl cholesterol (DC-Chol)>DOPE/dimyristoyltrimethylammonium propane. The replacement of DOPE by dipalmitoylphosphatidylcholine (DPPC) or the incorporation of dipamitoylphosphatidylethanolamine-PEG2000 (DPPE-PEG2000) in DOPE/cationic lipids reduced the toxicity toward macrophages and restored the synthesis of PKC-dependent modulators. The incorporation of DNA, either as an antisense oligonucleotide (15-mers) or as the plasmid vector pBR322 (4363 bp), in cationic liposomes did not reduce these adverse effects. These results, in addition to the observation that cationic liposomes are extremely toxic following oral administration indicate that DOPE/cationic lipid liposomes are not appropriate for DNA (or drug) delivery.

CC 63-5 (Pharmaceuticals)

IT **Drug delivery systems**
(liposomes, cationic; major limitations in the use of cationic liposomes for DNA delivery)

IT **DNA**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(major limitations in the use of cationic liposomes for DNA delivery)

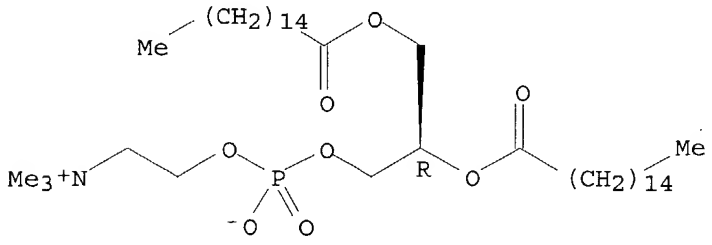
IT **63-89-8**, Dipalmitoylphosphatidylcholine 3700-67-2, Dimethyldioctadecylammonium bromide 25322-68-3D, reaction products with dipalmitoylphosphatidylethanolamine **72719-83-6** **113669-21-9** 137056-72-5 145035-97-8D, ethoxylated
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(major limitations in the use of cationic liposomes for DNA delivery)

IT **63-89-8**, Dipalmitoylphosphatidylcholine **72719-83-6** **113669-21-9**
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(major limitations in the use of cationic liposomes for DNA delivery)

RN 63-89-8 HCAPLUS

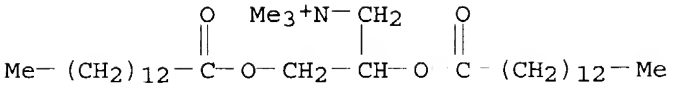
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 72719-83-6 HCAPLUS

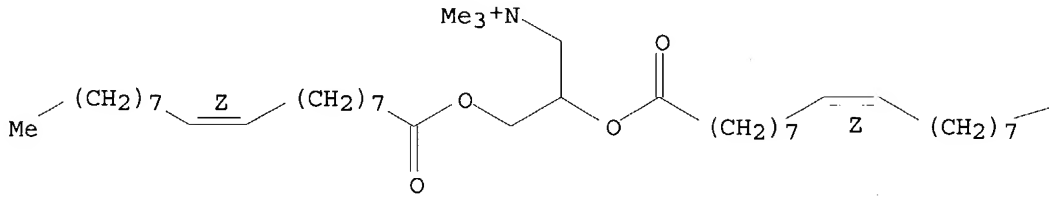
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(1-oxotetradecyl)oxy]- (9CI) (CA INDEX NAME)



RN 113669-21-9 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 50 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:1565 HCAPLUS
DOCUMENT NUMBER: 128:66511
TITLE: Increased efficiency of delivery of antisense nucleic acids using neutral phospholipid liposomes
INVENTOR(S): Klimuk, Sandra K.; Semple, Sean C.; Scherrer, Peter; Hope, Michael J.
PATENT ASSIGNEE(S): University of British Columbia, Can.
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9746671	A1	19971211	WO 1997-CA347	19970522
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 906421	A1	19990407	EP 1997-921565	19970522

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI
JP 2000511541 T2 20000905 JP 1998-500030 19970522
PRIORITY APPLN. INFO.: US 1996-657753 A 19960530
WO 1997-CA347 W 19970522

AB The efficiency of delivery of antisense nucleic acids to damaged tissues is increased by using neutral lipid-based liposomes. Neutral phospholipid liposomes do not activate complement and so avoid some of the toxicity problems associated with cationic lipids. The lipids used include at least two members selected from the group consisting of phospholipids, sterols and cationic lipids. In particular, methods for the delivery of antisense DNA to ICAM-1 to sites of inflammation are described.

IC ICM C12N015-11
ICS A61K009-127; A61K031-70; C07H021-00; C12N015-88

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 3

IT **Antisense DNA**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(increased efficiency of delivery of antisense nucleic acids using neutral phospholipid liposomes)

IT **Drug delivery systems**
(liposomes; increased efficiency of delivery of antisense nucleic acids using neutral phospholipid liposomes)

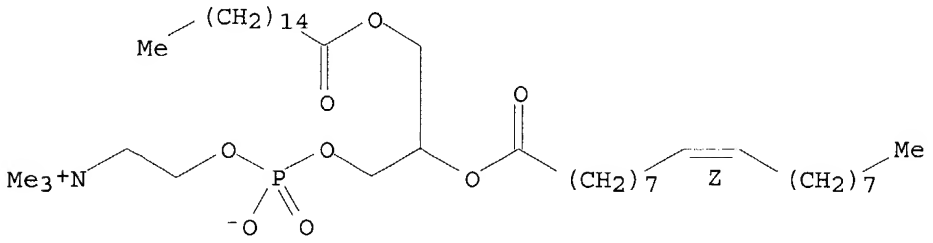
IT **Drug targeting**
(of liposomes, passive; increased efficiency of delivery of antisense nucleic acids using neutral phospholipid liposomes)

IT 2390-68-3, DDAB 2462-63-7, DOPE 7212-69-3 **26662-91-9**, POPC **104162-48-3**, DOTMA 124050-77-7, DOGS **144189-73-1**, DOTAP **168479-03-6**, DOSPA
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in neutral liposomes; increased efficiency of delivery of antisense nucleic acids using neutral phospholipid liposomes)

IT **26662-91-9**, POPC **104162-48-3**, DOTMA **144189-73-1**, DOTAP **168479-03-6**, DOSPA
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in neutral liposomes; increased efficiency of delivery of antisense nucleic acids using neutral phospholipid liposomes)

RN 26662-91-9 HCAPLUS
CN 3,5,8-Trioxa-4-phosphahexacos-17-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-9-oxo-7-[[(1-oxohexadecyl)oxy]methyl]-, inner salt, 4-oxide, (17Z)- (9CI) (CA INDEX NAME)

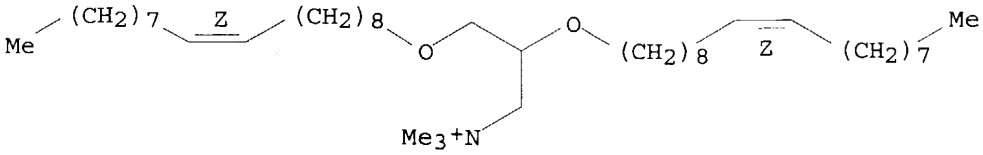
Double bond geometry as shown.



RN 104162-48-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride

(9CI) (CA INDEX NAME)

Double bond geometry as shown.



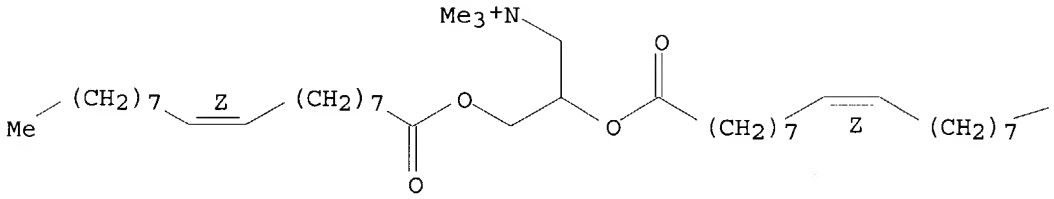
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

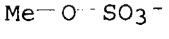
PAGE 1-A



PAGE 1-B

CM 2

CRN 21228-90-0
CMF C H3 O4 S



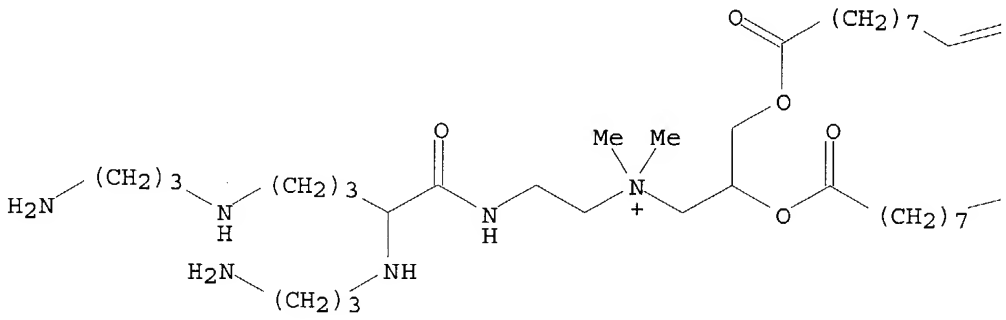
RN 168479-03-6 HCAPLUS
CN 1-Propanaminium, N-[2-[[2,5-bis[(3-aminopropyl)amino]-1-oxopentyl]amino]ethyl]-N,N-dimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, salt with trifluoroacetic acid (1:1) (9CI) (CA INDEX NAME)

CM 1

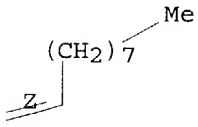
CRN 168479-02-5
CMF C54 H107 N6 O5

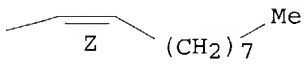
Double bond geometry as shown.

PAGE 1-A



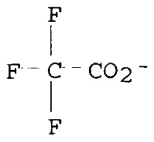
PAGE 1-B





CM 2

CRN 14477-72-6
CMF C2 F3 O2



L52 ANSWER 51 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:807853 HCAPLUS
DOCUMENT NUMBER: 128:158830
TITLE: Electrostatic and structural properties of complexes involving plasmid DNA and cationic lipids commonly used for gene delivery
AUTHOR(S): Zuidam, Nicolaas J.; Barenholz, Yechezkel
CORPORATE SOURCE: P.O. Box, Department of Biochemistry, The Hebrew University-Hadassah Medical School, Jerusalem 91120, 12272, Israel
SOURCE: Biochimica et Biophysica Acta (1998), 1368(1), 115-128
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study is aimed to characterize the interactions between plasmid DNA and cationic, large unilamellar vesicles, 110±20 nm in size, composed of lipids commonly used for transfections including DOTAP/DOPE (mole ratio 1/1), DOTAP/DOPC (mole ratio 1/1), 100 DOTAP, or DC-CHOL/DOPE (mole ratio 1/1). [Abbreviations: DOTAP, N-(1-(2,3-dioleoyloxy)propyl)-N,N,N-trimethylammonium chloride; DOPE, 1,2-dioleoyl-sn-glycero-3-phosphatidyl-ethanolamine; DOPC, 1,2-dioleoyl-sn-glycero-3-phosphatidylcholine; DC-CHOL, 3β-[N-(N',N'-dimethylaminoethane)carbamoyl] cholesterol]. A novel approach of combining Gouy-Chapman calcns. and fluorescence measurements of the pH at the surface of lipid assemblies by the fluorophore 4-heptadecyl-7-hydroxycoumarin showed that electrostatic parameters played a key role in the instantaneous formation of the DNA-lipid complexes upon addition of different amts. of plasmid DNA to cationic liposomes in 20 mM Hepes buffer (pH 7.4). Addition of large amts. of plasmid DNA leads to neutralization of 60 of the protonated DC-CHOL in DC-CHOL/DOPE (1/1) assemblies and 80 of the DOTAP in lipid assemblies. The characterization of these electrostatic parameters of the complexes suggests better and closer surrounding of plasmid DNA by lipids when DOPE is present. Time-dependent static light-scattering measurements monitored the formation of complexes and also showed that these complexes were highly unstable with respect to size at DNA/cationic lipid molar ratios between 0.2 and 0.8.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 3

IT **Drug delivery systems**
(cationic lipid unilamellar vesicles; electrostatic and structural properties of complexes involving plasmid DNA and cationic lipids commonly used for gene delivery)

IT Gene therapy
Plasmids
Transformation, genetic
(electrostatic and structural properties of complexes involving plasmid DNA and cationic lipids commonly used for gene delivery)

IT **DNA**

RL: PEP (Physical, engineering or chemical process); PROC (Process)
(electrostatic and structural properties of complexes involving plasmid DNA and cationic lipids commonly used for gene delivery)

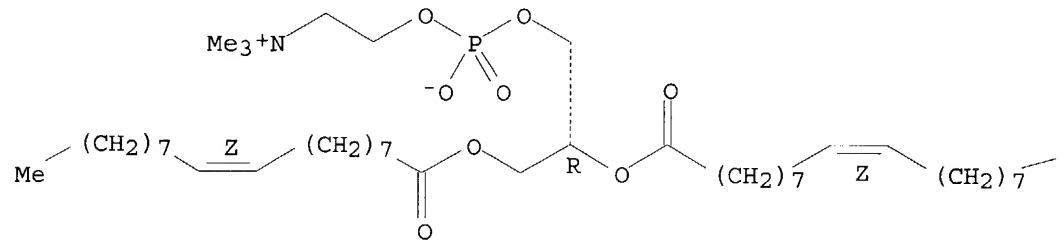
IT 2462-63-7, DOPE **4235-95-4**, DOPC **132172-61-3**, DOTAP
137056-72-5
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(electrostatic and structural properties of complexes involving plasmid DNA and cationic lipids commonly used for gene delivery)

IT **4235-95-4**, DOPC **132172-61-3**, DOTAP
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(electrostatic and structural properties of complexes involving plasmid DNA and cationic lipids commonly used for gene delivery)

RN 4235-95-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



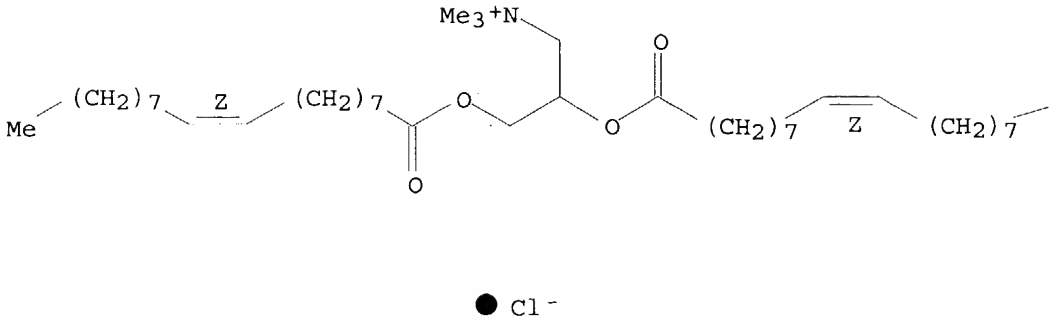
PAGE 1-B

Me

RN 132172-61-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 52 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:601244 HCAPLUS
DOCUMENT NUMBER: 127:302928
TITLE: Toxicity and immunomodulatory activity of liposomal vectors formulated with cationic lipids toward immune effector cells
AUTHOR(S): Filion, Mario C.; Phillips, Nigel C.
CORPORATE SOURCE: Faculte de Pharmacie, C.P. 6128 Succ. Centre-Ville, Universite de Montreal, Montreal, Que., Can.
SOURCE: Biochimica et Biophysica Acta (1997), 1329(2), 345-356
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Liposomal vectors formulated with cationic lipids (cationic liposomes) and fusogenic dioleoylphosphatidylethanolamine (DOPE) have potential for modulating the immune system by delivering gene or antisense oligonucleotide inside immune cells. The toxicity and the immunoadjuvant activity of cationic liposomes containing nucleic acids toward immune effector cells has not been investigated in detail. In this report, we have evaluated the toxicity of liposomes formulated with various cationic lipids towards murine macrophages and T lymphocytes and the human monocyte-like U937 cell line. The effect of these cationic liposomes on the synthesis of two immunomodulators produced by activated macrophages, nitric oxide (NO) and tumor necrosis factor-α (TNF-α), has also been determined We have found that liposomes formulated from DOPE and cationic lipids based on diacyltrimethylammonium propane (dioleoyl-, dimyristoyl-, dipalmitoyl-, disteroyl-: DOTAP, DMTAP, DPTAP, DSTAP) or dimethyldioctadecylammonium bromide (DDAB) are highly toxic in vitro toward phagocytic cells (macrophages and U937 cells), but not towards

non-phagocytic T lymphocytes. The rank order of toxicity was DOPE/DDAB>DOPE/DOTAP>DOPE/DMTAP>DOPE/DPTAP>DOPE/DSTAP. The ED50's for macrophage toxicity were <10 nmol/mL for DOPE/DDAB, 12 nmol/mL for DOPE/DOTAP, 50 nmol/mL for DOPE/DMTAP, 400 nmol/mL for DOPE/DPTAP and >1000 nmol/mL for DOPE/DSTAP. The incorporation of DNA (antisense oligonucleotide or plasmid vector) into the cationic liposomes marginally reduced their toxicity towards macrophages. Although toxicity was observed with cationic lipids alone, it was clearly enhanced by the presence of DOPE. The replacement of DOPE by dipalmitoylphosphatidylcholine (DPPC) significantly reduced liposome toxicity towards macrophages, and the presence of dipalmitoylphosphatidylethanolamine-PEG2000 (DPPE-PEG2000: 10 mol%) in the liposomes completely abolished this toxicity. Cationic liposomes, irresp. of their DNA content, down-regulated NO and TNF-α synthesis by lipopolysaccharide (LPS)/interferon-γ (IFN-γ)-activated macrophages. The replacement of DOPE by DPPC, or the addition of DPPE-PEG2000, restored NO and TNF-α synthesis by activated macrophages. Since macrophages constitute the major site of liposome localization after parenteral administration and play an important role in the control of the immune system, cationic liposomes should be used with caution to deliver gene or antisense oligonucleotide to mammalian cells. Cationic lipids show in vitro toxicity toward phagocytic cells and inhibit in vitro and in situ NO and TNF-α production by activated macrophages.

CC 1-4 (Pharmacology)
Section cross-reference(s): 63

IT **Drug delivery systems**
(liposomes, cationic liposomes; toxicity and immunomodulatory activity of liposomal vectors formulated with cationic lipids toward immune effector cells)

IT **Antisense oligonucleotides**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(toxicity and immunomodulatory activity of liposomal vectors formulated with cationic lipids toward immune effector cells)

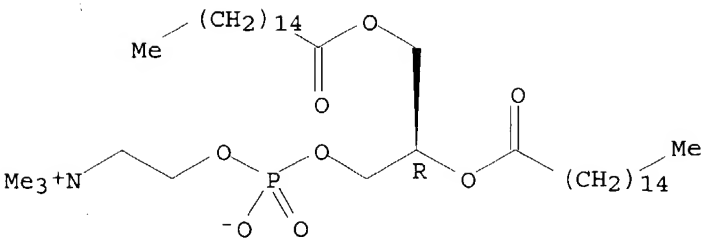
IT **63-89-8**, Dipalmitoylphosphatidylcholine 3700-67-2, Dimethyldioctadecylammonium bromide 5681-36-7, Dipalmitoylphosphatidylethanolamine **72719-83-6** **113669-21-9** **138915-91-0**
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(toxicity and immunomodulatory activity of liposomal vectors formulated with cationic lipids toward immune effector cells)

IT **63-89-8**, Dipalmitoylphosphatidylcholine **72719-83-6** **113669-21-9** **138915-91-0**
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(toxicity and immunomodulatory activity of liposomal vectors formulated with cationic lipids toward immune effector cells)

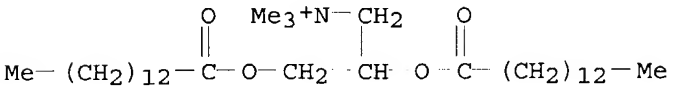
RN 63-89-8 HCAPLUS

CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



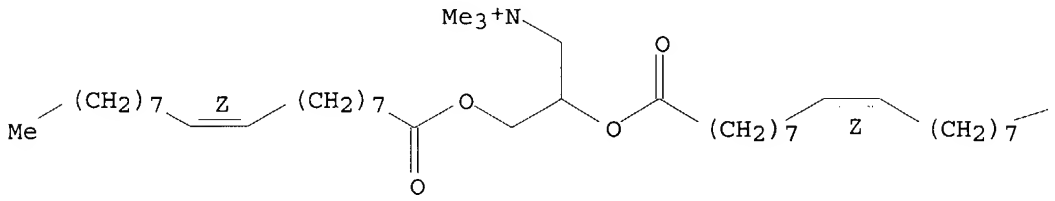
RN 72719-83-6 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(1-oxotetradecyl)oxy]- (9CI) (CA INDEX NAME)



RN 113669-21-9 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]- (9CI) (CA INDEX NAME)

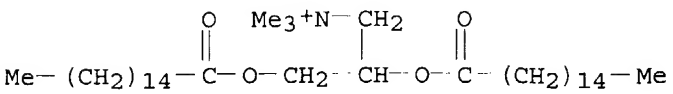
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

RN 138915-91-0 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(1-oxohexadecyl)oxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 53 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:247860 HCAPLUS
DOCUMENT NUMBER: 126:229615
TITLE: Enhanced artificial viral envelopes for cellular delivery of therapeutic substances
INVENTOR(S): Conary, Jon T.; Schreier, Hans
PATENT ASSIGNEE(S): Advanced Therapies, Inc., USA; Conary, Jon T.; Schreier, Hans
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9704748	A2	19970213	WO 1996-US12750	19960801
WO 9704748	A3	19970529		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
AU 9666914	A1	19970226	AU 1996-66914	19960801

PRIORITY APPLN. INFO.:

US 1995-1738P	P	19950801
US 1995-2580P	P	19950821
US 1995-690613	A2	19960731
US 1996-690613	A	19960731
WO 1996-US12750	W	19960801

AB This invention provides artificial viral envelopes and other lipid vesicles that encapsulate therapeutic substances, such as expression vectors, targeted to mammalian cells. Polynucleotides may be packed into the envelopes by compressing them beforehand with a short peptide with a predominant pos. charge. The compression step not only facilitates encapsulation, it also increases the number of vesicles containing nucleic acid, minimizes the amount of free nucleic acid, and may also increase the size and complexity of plasmids that can be encapsulated. The vesicles may be provided with a tissue-targeting component that helps direct it towards certain tissue sites in an animal. The vesicles may also be provided with a fusogenic component that facilitates delivery of the therapeutic substance into the cell. The materials and reagents of this invention are effective, for example, in increasing expression of model proteins in both isolated cells and intact animals, and are expected to be useful for gene therapy.

IC ICM A61K009-127
ICS C12N015-88
CC 63-5 (Pharmaceuticals)
IT **Drug delivery systems**
Gene therapy
Genetic vectors
Plasmids
Protein sequences

Transformation, genetic
cDNA sequences
(enhanced artificial viral envelopes for cellular delivery of therapeutic substances)

IT Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphatidylserines
Phospholipids, biological studies
Polynucleotides
Proteins, general, biological studies
Reporter gene
Sphingomyelins
Toxins
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enhanced artificial viral envelopes for cellular delivery of therapeutic substances)

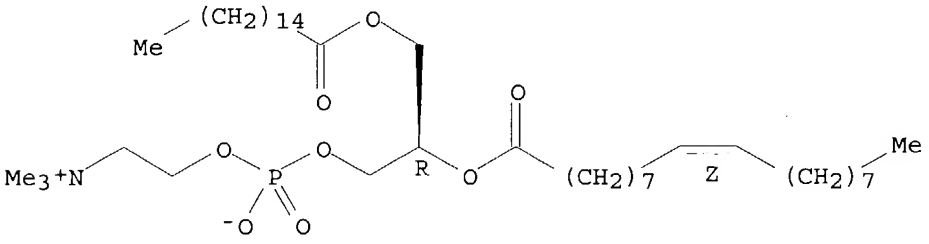
IT **Drug delivery systems**
(liposomes; enhanced artificial viral envelopes for cellular delivery of therapeutic substances)

IT 50-67-9D, Serotonin, lipid derivs. 57-88-5, Cholesterol, biological studies 361-09-1, Sodium cholate 2462-63-7, DOPE **26853-31-6**, Popc **128835-92-7**, Lipofectin 137056-72-5
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enhanced artificial viral envelopes for cellular delivery of therapeutic substances)

IT **26853-31-6**, Popc **128835-92-7**, Lipofectin
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enhanced artificial viral envelopes for cellular delivery of therapeutic substances)

RN 26853-31-6 HCAPLUS
CN 3,5,8-Trioxa-4-phosphahexacos-17-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-9-oxo-7-[[(1-oxohexadecyl)oxy]methyl]-, inner salt, 4-oxide, (7R,17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

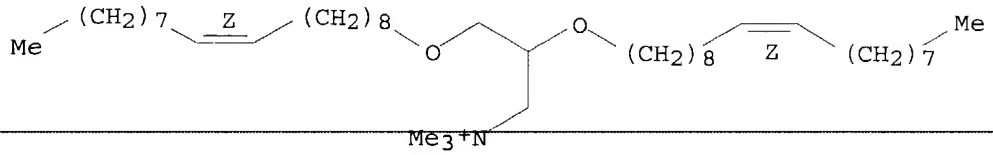


RN 128835-92-7 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 104162-48-3
CMF C42 H84 N O2 . Cl

Double bond geometry as shown.

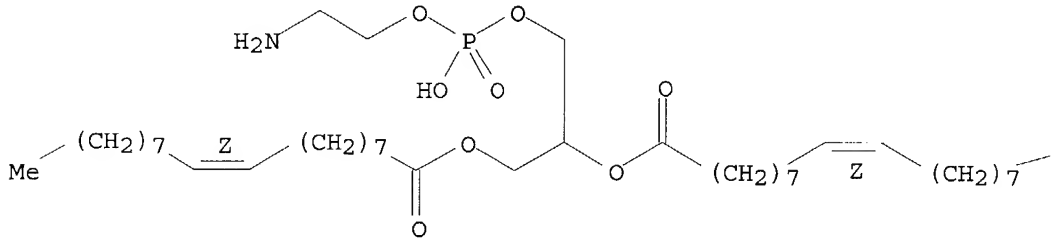


CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

L52 ANSWER 54 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:185198 HCAPLUS
DOCUMENT NUMBER: 126:272297
TITLE: Pulmonary surfactant inhibits cationic liposome-mediated gene delivery to respiratory epithelial cells in vitro
AUTHOR(S): Ducan, James E.; Whitsett, Jeffrey A.; Horowitz, Ann D.

CORPORATE SOURCE: Duke University School of Medicine, Durham, NC, 27710, USA
SOURCE: Human Gene Therapy (1997), 8(4), 431-438
CODEN: HGTHE3; ISSN: 1043-0342
PUBLISHER: Liebert
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cationic lipid-mediated transfection of the alveolar epithelium in vivo will require exposure of plasmid DNA and cationic lipids to endogenous surfactant lipids and proteins in the alveolar space. Effects of pulmonary surfactant and of surfactant constituents on transfection in vitro of two respiratory epithelial cells lines (MLE-15 and H441) with a plasmid encoding the luciferase reporter gene were studied using two cationic lipid formulations: 1,2-dimyristyloxypropyl-3-dimethyl-hydroxyethyl ammonium bromide/cholesterol (DMRIE/C) and 1,2-dioleoyl-3-trimethylammonium propane/dioleoyl phosphatidylethanolamine (DOTAP/DOPE). Gene expression, as assessed luciferase activity, decreased as increasing concns. of natural surfactant were added to cationic lipid-DNA complexes. Incorporation of phospholipids DOPC/DOPG or surfactant proteins SP-B or SP-C in the cationic lipid formulation inhibited transfection. A fluorescent lipid mixing assay was used to determine the effects of surfactant proteins SP-B and SP-C on mixing between cationic lipid-DNA complexes and surfactant lipid vesicles. Mixing between DOPC/DOPG vesicles and cationic lipid-DNA complexes in the absence of added proteins amounted to 10-20%. Addition of SP-B or SP-C increased the mixing of DOPC/DOPG vesicles with DOTAP/DOPE-DNA complexes, but not DMRIE/C-DNA complexes. These results demonstrate that pulmonary surfactant lipids and proteins inhibit transfection with cationic lipid-DNA complexes in vitro, and may therefore represent a barrier to gene transfer in the lung.

CC 1-12 (Pharmacology)
Section cross-reference(s): 63

IT **Drug delivery systems**
(liposomes; pulmonary surfactant and surfactant proteins inhibit cationic liposome-mediated gene delivery to respiratory epithelial cells in vitro)

IT Gene therapy
Plasmid vectors
Plasmids
Pulmonary surfactant
Transduction, genetic
(pulmonary surfactant and surfactant proteins inhibit cationic liposome-mediated gene delivery to respiratory epithelial cells in vitro)

IT 62700-69-0, Dioleoyl phosphatidylglycerol **68737-67-7**, Dioleoyl phosphatidylcholine
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(pulmonary surfactant and surfactant proteins inhibit cationic liposome-mediated gene delivery to respiratory epithelial cells in vitro)

IT 57-88-5, Cholesterol, biological studies 2462-63-7, Dioleoyl phosphatidylethanolamine **113669-21-9 153312-64-2**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pulmonary surfactant and surfactant proteins inhibit cationic liposome-mediated gene delivery to respiratory epithelial cells in vitro)

IT **68737-67-7**, Dioleoyl phosphatidylcholine
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(pulmonary surfactant and surfactant proteins inhibit cationic

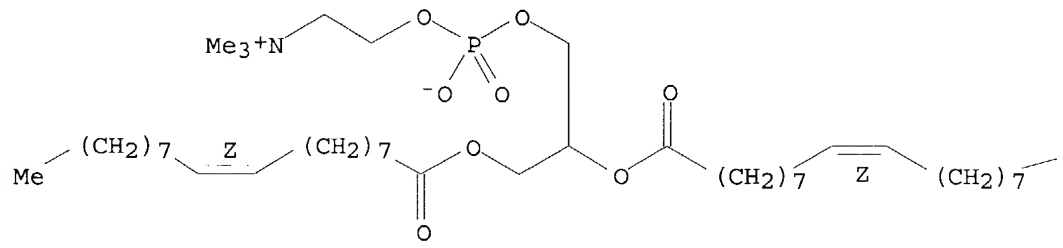
liposome-mediated gene delivery to respiratory epithelial cells in vitro)

RN 68737-67-7 HCAPLUS

CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (18Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

IT **113669-21-9 153312-64-2**

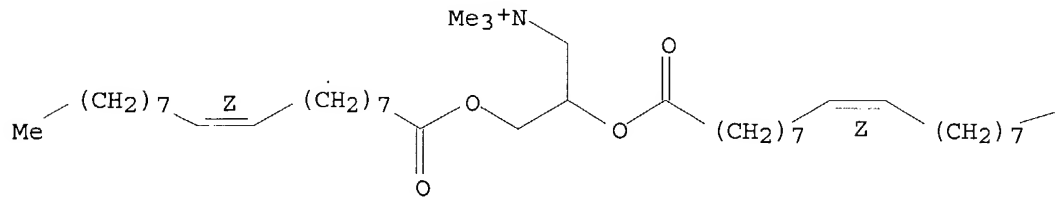
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pulmonary surfactant and surfactant proteins inhibit cationic liposome-mediated gene delivery to respiratory epithelial cells in vitro)

RN 113669-21-9 HCAPLUS

CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-(9CI) (CA INDEX NAME)

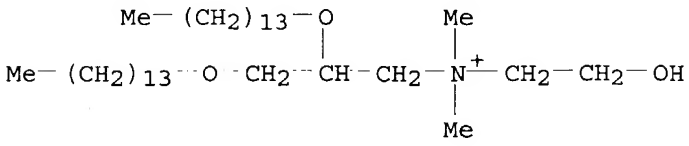
Double bond geometry as shown.

PAGE 1-A



Me

RN 153312-64-2 HCAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



● Br^-

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 55 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:134871 HCAPLUS
DOCUMENT NUMBER: 126:148488
TITLE: Separation of active complexes from mixtures of polynucleotides associated with transfecting components
INVENTOR(S): Skoza, Francis C., Jr.; Xu, Yuhong; Wang, Jinkang
PATENT ASSIGNEE(S): Regents of the University of California, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640264	A1	19961219	WO 1996-US7824	19960528
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
US 5972600	A	19991026	US 1995-482110	19950607
AU 9660248	A1	19961230	AU 1996-60248	19960528
AU 714526	B2	20000106		
EP 831923	A1	19980401	EP 1996-917839	19960528
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

JP 2001517061 T2 20011002 JP 1997-500774 19960528
PRIORITY APPLN. INFO.: US 1995-482110 A 19950607
US 1992-864876 B2 19920403
US 1992-913669 B2 19920714
US 1993-92200 B2 19930714
WO 1996-US7824 W 19960528

AB The invention separates defined, active complexes that share a particular physicochem. characteristic such as d., surface charge or particle size from complexes formed by the association of a polynucleotide with a transfecting component that increases transfection activity, such as a lipid, cationic lipid, liposome, peptide, cationic peptide, dendrimer or polycation. In a preferred embodiment, polynucleotide-transfecting component complexes are ultracentrifuged to resolve one or more bands corresponding to complexes having a specific polynucleotide-transfecting component interaction. Polynucleotide complexes having a cationic liposome transfecting component resolve into two primary bands corresponding to complexes formed either under excess lipid conditions or under excess polynucleotide conditions. In an alternate embodiment, polynucleotide-transfecting component complexes are resolved using cross-flow electrophoresis in identify complexes having specific interactions and to sep. them from excess initial components. This invention is of relevance to delivery of polynucleotides for gene therapy.

IC ICM A61K048-00
ICS C12Q001-68

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 3

IT **Drug delivery systems**
(liposomes, cationic; separation of active complexes from mixts. of polynucleotides associated with transfecting components)

IT **Polynucleotides**
RL: REM (Removal or disposal); PROC (Process)
(separation of active complexes from mixts. of polynucleotides associated with
transfecting components)

IT 57-09-0, 1-Hexadecanaminium, N,N,N-trimethyl-, bromide 57-88-5, Cholesterol, biological studies 124-03-8, Cetyldimethylethylammonium bromide 406-76-8D, 1-Propanaminium, 3-carboxy-2-hydroxy-N,N,N-trimethyl-, inner salt, lipid esters 541-15-1D, Carnitine, lipid esters 2462-63-7, DOPE 3700-67-2, Dimethyldioctadecylammonium bromide **4235-95-4**, Dopc 25496-72-4, Monooleoyl glycerol **104162-48-3**, Dotma 124050-77-7, DOGS **144189-73-1**, Dotap **153312-64-2**, Dmrie **168479-03-6**, DOSPA 183283-19-4 183283-20-7 186584-03-2 186584-04-3 186584-06-5 186584-08-7 186584-10-1 186589-48-0 186589-50-4 186589-52-6 186589-60-6 186589-62-8 186589-64-0 186589-66-2 186589-68-4 186589-70-8 186589-72-0
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(separation of active complexes from mixts. of polynucleotides associated with
transfecting components)

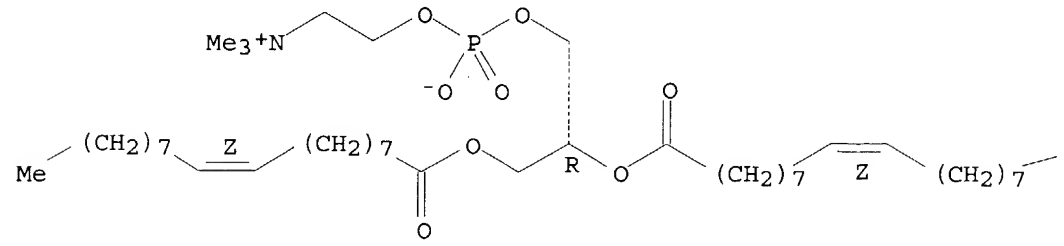
IT **4235-95-4**, Dopc **104162-48-3**, Dotma **144189-73-1**, Dotap **153312-64-2**, Dmrie **168479-03-6**, DOSPA
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(separation of active complexes from mixts. of polynucleotides associated with
transfecting components)

RN 4235-95-4 HCAPLUS

CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (7R,18Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

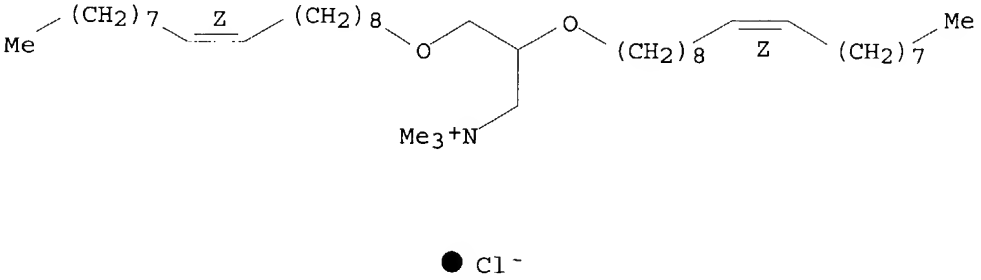
PAGE 1-A



PAGE 1-B

RN 104162-48-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



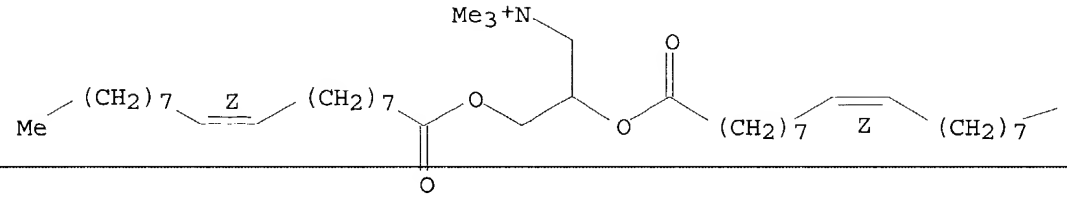
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

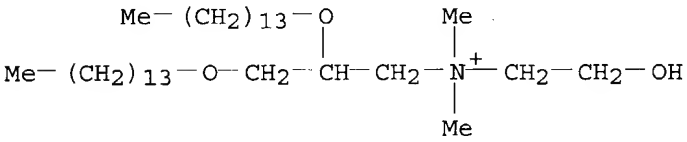
Me

CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO_3^-

RN 153312-64-2 HCAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



● Br^-

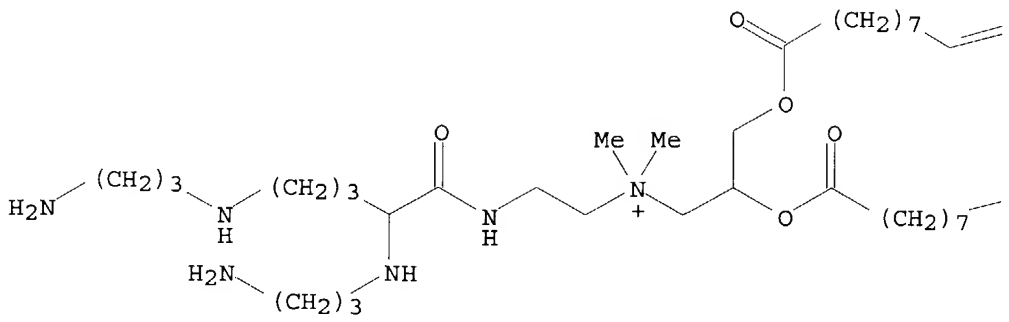
RN 168479-03-6 HCAPLUS
CN 1-Propanaminium, N-[2-[[2,5-bis[(3-aminopropyl)amino]-1-oxopentyl]amino]ethyl]-N,N-dimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, salt with trifluoroacetic acid (1:1) (9CI) (CA INDEX NAME)

CM 1

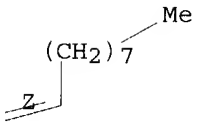
CRN 168479-02-5
CMF C54 H107 N6 O5

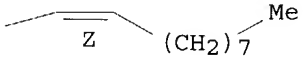
Double bond geometry as shown.

PAGE 1-A



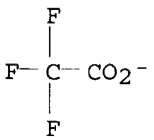
PAGE 1-B





CM 2

CRN 14477-72-6
CMF C2 F3 O2



L52 ANSWER 56 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:48717 HCAPLUS
DOCUMENT NUMBER: 126:54891
TITLE: Nucleic acid ligand complexes
INVENTOR(S): Gold, Larry; Schmidt, Paul G.; Janjic, Nebojsa
PATENT ASSIGNEE(S): Nexstar Pharmaceuticals, Inc., USA; Gold, Larry; Schmidt, Paul G.; Janjic, Nebojsa
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 127
PATENT INFORMATION:

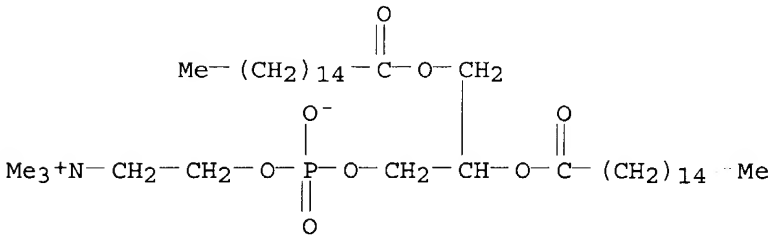
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9634876	A1	19961107	WO 1996-US6171	19960502
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 6011020	A	20000104	US 1995-434465	19950504
AU 9657231	A1	19961121	AU 1996-57231	19960502
AU 728176	B2	20010104		
EP 824541	A1	19980225	EP 1996-915463	19960502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11504926	T2	19990511	JP 1996-533500	19960502
US 6147204	A	20001114	US 1997-945604	19971028
US 6465188	B1	20021015	US 2000-569572	20000510
US 2003125263	A1	20030703	US 2002-261159	20020930

PRIORITY APPLN. INFO.:
US 1995-434465 A 19950504
US 1995-464443 A 19950605
US 1990-536428 B2 19900611
US 1991-714131 A2 19910610
US 1994-234997 A2 19940428
WO 1996-US6171 W 19960502
US 1997-945604 A3 19971028
US 2000-569572 A1 20000510

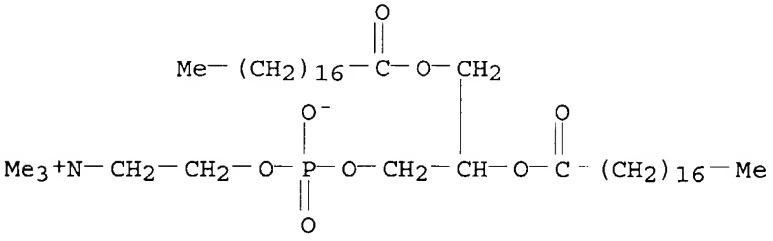
AB This invention discloses a method for preparing a therapeutic or diagnostic complex comprised of a nucleic acid ligand and a lipophilic compound or non-immunogenic, high mol. weight compound by identifying a nucleic acid ligand by SELEX (Systematic Evolution of Ligands by EXponential enrichment) methodol. and associating the nucleic acid ligand with a lipophilic compound or a non-immunogenic, high mol. weight compound The invention further discloses complexes comprising one or more nucleic acid ligands in association with a lipophilic compound or non-immunogenic, high mol. weight compound

IC ICM C07H021-02
ICS C07H021-04; C12P019-34; C12Q001-68
CC 1-12 (Pharmacology)
Section cross-reference(s): 33
IT **Drug delivery systems**
(liposomes; nucleic acid ligand complexes for diagnostic and therapeutic purposes)
IT Ligands
Nucleic acids
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES

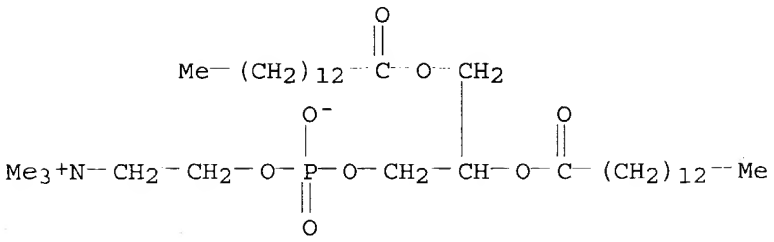
(Uses)
(nucleic acid ligand complexes for diagnostic and therapeutic purposes)
IT **2644-64-6**, Dipalmitoylphosphatidylcholine **4539-70-2**, Distearoylphosphatidylcholine **18656-38-7**, Dimyristoylphosphatidylcholine **144189-73-1**, Dotap
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(nucleic acid ligand complexes for diagnostic and therapeutic purposes)
IT **2644-64-6**, Dipalmitoylphosphatidylcholine **4539-70-2**, Distearoylphosphatidylcholine **18656-38-7**, Dimyristoylphosphatidylcholine **144189-73-1**, Dotap
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(nucleic acid ligand complexes for diagnostic and therapeutic purposes)
RN 2644-64-6 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 4539-70-2 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 18656-38-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatricosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxotetradecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



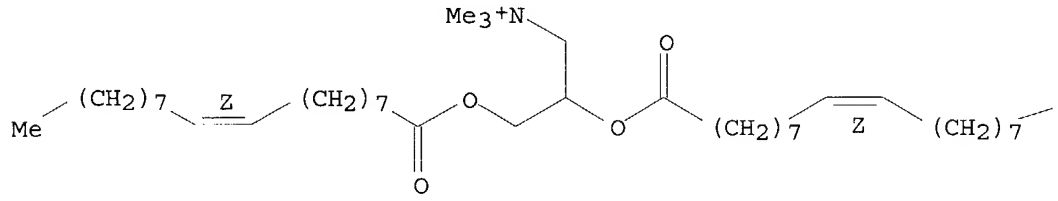
RN 144189-73-1 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-, methyl sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 113669-21-9
CMF C42 H80 N O4

Double bond geometry as shown.

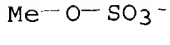
PAGE 1-A



PAGE 1-B

CM 2

CRN 21228-90-0
CMF C H3 O4 S



L52 ANSWER 57 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:15526 HCAPLUS

DOCUMENT NUMBER: 126:79951
TITLE: Therapeutic drug delivery systems comprising gas-filled microspheres
INVENTOR(S): Unger, Evan C.; Fritz, Thomas A.; Matsunaga, Terry; Ramaswami, Varadarajan; Yellowhair, David; Wu, Guanli
PATENT ASSIGNEE(S): ImaRx Pharmaceutical Corp., USA
SOURCE: U.S., 48 pp., Cont.-in-part of U.S. Ser. No. 716,889,abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5580575	A	19961203	US 1993-76250	19930611
US 5088499	A	19920218	US 1990-569828	19900820
WO 9109629	A1	19910711	WO 1990-US7500	19901219
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AT 180170	E	19990615	AT 1991-902857	19901219
ES 2131051	T3	19990716	ES 1991-902857	19901219
JP 3309356	B2	20020729	JP 1991-503276	19901219
JP 05502675	T2	19930513		
US 5228446	A	19930720	US 1991-717084	19910618
WO 9222247	A1	19921223	WO 1992-US2615	19920331
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9220020	A1	19930112	AU 1992-20020	19920331
AU 667471	B2	19960328		
JP 06508364	T2	19940922	JP 1993-500847	19920331
JP 3456584	B2	20031014		
EP 616508	A1	19940928	EP 1992-912456	19920331
EP 616508	B1	20010718		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
AT 203148	E	20010815	AT 1992-912456	19920331
ES 2159280	T3	20011001	ES 1992-912456	19920331
US 5348016	A	19940920	US 1993-88268	19930707
US 5542935	A	19960806	US 1993-160232	19931130
US 5769080	A	19980623	US 1994-199462	19940222
CN 1125394	A	19960626	CN 1994-192404	19940501
WO 9428873	A1	19941222	WO 1994-US5620	19940512
W: AU, CA, CN, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9470948	A1	19950103	AU 1994-70948	19940512
AU 684088	B2	19971204		
EP 707471	A1	19960424	EP 1994-920019	19940512
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2164843	AA	19941222	CA 1994-2164843	19940519
CA 2164846	AA	19941222	CA 1994-2164846	19940519
WO 9428874	A1	19941222	WO 1994-US5633	19940519
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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9469537	A1	19950103	AU 1994-69537	19940519
AU 696056	B2	19980827		
CN 1125393	A	19960626	CN 1994-192403	19940519
JP 08511523	T2	19961203	JP 1995-501811	19940519
JP 09501410	T2	19970210	JP 1995-501807	19940519

EP 802788	A1	19971029	EP 1994-918051	19940519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 5773024	A	19980630	US 1994-307305	19940916
US 5733572	A	19980331	US 1994-346426	19941129
US 5922304	A	19990713	US 1995-401974	19950309
US 5705187	A	19980106	US 1995-417238	19950405
US 5571497	A	19961105	US 1995-468056	19950606
US 5656211	A	19970812	US 1995-482294	19950607
US 5770222	A	19980623	US 1995-472305	19950607
US 6443898	B1	20020903	US 1995-485998	19950607
CN 1180310	A	19980429	CN 1996-193069	19960327
CN 1102045	B	20030226		
US 6001335	A	19991214	US 1996-665719	19960618
US 6146657	A	20001114	US 1996-741598	19961101
US 5935553	A	19990810	US 1996-758179	19961125
US 6039557	A	20000321	US 1997-833489	19970407
US 5985246	A	19991116	US 1997-888426	19970708
AU 9856271	A1	19980507	AU 1998-56271	19980224
AU 713127	B2	19991125		
US 6551574	B1	20030422	US 1998-52075	19980331
AU 9888406	A1	19990204	AU 1998-88406	19981009
AU 732440	B2	20010426		
HK 1013625	A1	20000420	HK 1998-114978	19981223
US 6315981	B1	20011113	US 1999-272468	19990319
GR 3036877	T3	20020131	GR 2001-401740	20011011

PRIORITY APPLN. INFO.:

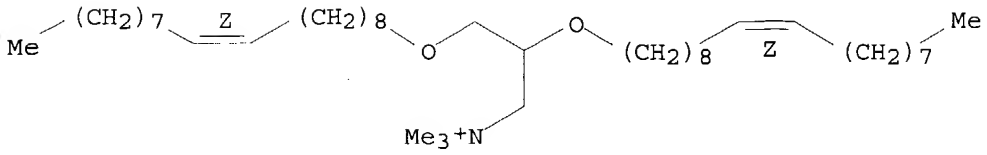
US 1989-455707	B2	19891222
US 1990-569828	A2	19900820
US 1991-716899	B2	19910618
US 1991-717084	A2	19910618
WO 1990-US7500	W	19901219
US 1991-716793	A	19910618
US 1991-750877	A3	19910826
US 1992-818069	A3	19920108
WO 1992-US2615	A	19920331
US 1992-967974	A3	19921027
US 1993-17683	A3	19930212
US 1993-18112	B3	19930217
US 1993-76239	A2	19930611
US 1993-76250	A2	19930611
US 1993-85608	A3	19930630
US 1993-88268	A3	19930707
US 1993-159674	B2	19931130
US 1993-159687	A2	19931130
US 1993-160232	A	19931130
US 1993-163039	A3	19931206
US 1994-212553	B2	19940311
WO 1994-US5620	W	19940512
AU 1994-69537	A3	19940519
WO 1994-US5633	W	19940519
US 1994-307305	A2	19940916
US 1994-346426	A	19941129
US 1995-395683	A3	19950228
US 1995-401974	A3	19950309
US 1995-468056	A3	19950606
US 1995-471250	A3	19950606
US 1995-482294	A3	19950607
US 1996-665719	A3	19960618
US 1996-741598	A3	19961101

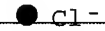
AB Therapeutic drug delivery systems comprise gas-filled impermeable

microspheres, e.g. liposomes, in which a drug is encapsulated. Such liposomes are especially useful for controlled delivery of genetic material in gene therapy, and of lipophilic drugs. The therapeutic agent is preferably released from the microspheres locally in a targeted manner, immediately or gradually, by application of ultrasound. Methods of and apparatus for preparing such liposomes and methods for employing such liposomes in drug delivery applications are also disclosed. For example, gas-filled liposomes are prepared by shaking an aqueous solution containing a lipid and a therapeutic compound in the presence of a gas at a temperature below the gel→liquid crystalline phase transition temperature of the lipid.

IC ICM A61K009-127
NCL 424450000
CC 63-6 (Pharmaceuticals)
IT **Histocompatibility antigens**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA-B7, gene for, liposomes containing; therapeutic drug delivery systems comprising gas-filled microspheres)
IT **Antisense oligonucleotides**
DNA
Gene, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing; therapeutic drug delivery systems comprising gas-filled microspheres)
IT **Drug delivery systems**
(liposomes; therapeutic drug delivery systems comprising gas-filled microspheres)
IT **Drug delivery systems**
(microspheres; therapeutic drug delivery systems comprising gas-filled microspheres)
IT **104162-48-3**, DOTMA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic, DNA-filled liposomes containing; therapeutic drug delivery systems comprising gas-filled microspheres)
IT **63-89-8** 124-38-9, Carbon dioxide, biological studies
816-94-4, DSPC 5681-36-7, Dipalmitoylphosphatidylethanolamine
7440-01-9, Neon, biological studies 7440-37-1, Argon, biological studies
7440-59-7, Helium, biological studies 7440-63-3, Xenon, biological studies 7727-37-9, Nitrogen, biological studies 7782-44-7, Oxygen, biological studies 25322-68-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic drug delivery systems comprising gas-filled microspheres)
IT **104162-48-3**, DOTMA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic, DNA-filled liposomes containing; therapeutic drug delivery systems comprising gas-filled microspheres)
RN 104162-48-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

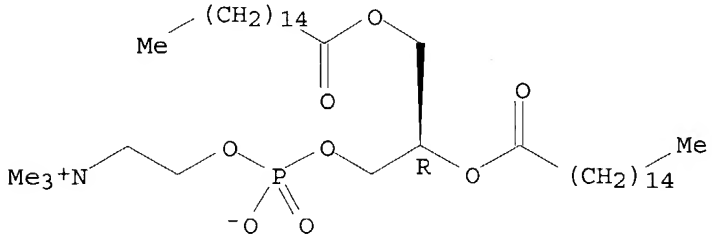
Double bond geometry as shown.





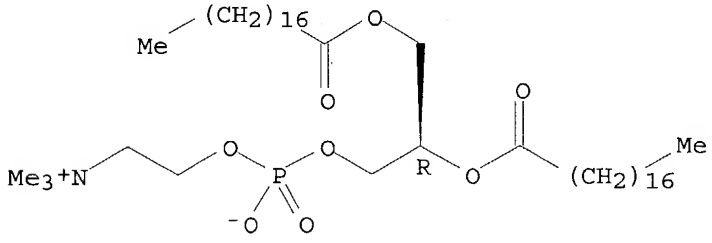
IT **63-89-8 816-94-4**, DSPC
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic drug delivery systems comprising gas-filled microspheres)
RN 63-89-8 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 816-94-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L52 ANSWER 58 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:535052 HCAPLUS
DOCUMENT NUMBER: 125:230795
TITLE: Therapeutic delivery systems comprising gaseous

precursor-filled liposomes
INVENTOR(S): Unger, Evan C.; Fritz, Thomas A.; Matsunaga, Terry; Ramaswami, Varadarajan; Yellowhair, David; Wu, Guanli
PATENT ASSIGNEE(S): ImaRx Pharmaceutical Corp., USA
SOURCE: U.S., 62 pp., Cont.-in-part of U.S. Ser. No. 159, 687.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5542935	A	19960806	US 1993-160232	19931130
US 5088499	A	19920218	US 1990-569828	19900820
WO 9109629	A1	19910711	WO 1990-US7500	19901219
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AT 180170	E	19990615	AT 1991-902857	19901219
ES 2131051	T3	19990716	ES 1991-902857	19901219
JP 3309356	B2	20020729	JP 1991-503276	19901219
JP 05502675	T2	19930513		
US 5228446	A	19930720	US 1991-717084	19910618
WO 9222247	A1	19921223	WO 1992-US2615	19920331
W: AU, CA, JP				
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AU 9220020	A1	19930112	AU 1992-20020	19920331
AU 667471	B2	19960328		
JP 06508364	T2	19940922	JP 1993-500847	19920331
JP 3456584	B2	20031014		
EP 616508	A1	19940928	EP 1992-912456	19920331
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AT 203148	E	20010815	AT 1992-912456	19920331
ES 2159280	T3	20011001	ES 1992-912456	19920331
US 5580575	A	19961203	US 1993-76250	19930611
US 5348016	A	19940920	US 1993-88268	19930707
US 5585112	A	19961217	US 1993-159687	19931130
US 5769080	A	19980623	US 1994-199462	19940222
CA 2164846	AA	19941222	CA 1994-2164846	19940519
WO 9428874	A1	19941222	WO 1994-US5633	19940519
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AU 696056	B2	19980827		
CN 1125393	A	19960626	CN 1994-192403	19940519
JP 08511523	T2	19961203	JP 1995-501811	19940519
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WO 9428780	A2	19941222	WO 1994-US5792	19940520
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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
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EP 712293	A1	19960522	EP 1994-919208	19940520
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CN 1125389	A	19960626	CN 1994-192402	19940520
CN 1125654	B	20031029		
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ES 2193161	T3	20031101	ES 1994-919208	19940520
US 5773024	A	19980630	US 1994-307305	19940916
US 5733572	A	19980331	US 1994-346426	19941129
CA 2177713	AA	19950608	CA 1994-2177713	19941130
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EP 740528	A1	19961106	EP 1995-908414	19941130
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AT 235228	E	20030415	AT 1995-908414	19941130
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US 5571497	A	19961105	US 1995-468056	19950606
US 5853752	A	19981229	US 1995-487230	19950606
US 5656211	A	19970812	US 1995-482294	19950607
US 6443898	B1	20020903	US 1995-485998	19950607
CN 1180310	A	19980429	CN 1996-193069	19960327
CN 1102045	B	20030226		
US 6001335	A	19991214	US 1996-665719	19960618
US 6146657	A	20001114	US 1996-741598	19961101
US 5935553	A	19990810	US 1996-758179	19961125
US 6039557	A	20000321	US 1997-833489	19970407
US 5985246	A	19991116	US 1997-888426	19970708
US 6071495	A	20000606	US 1997-942862	19971002
AU 9856271	A1	19980507	AU 1998-56271	19980224
AU 713127	B2	19991125		
US 6551574	B1	20030422	US 1998-52075	19980331
US 6479034	B1	20021112	US 1998-118329	19980717
AU 9888406	A1	19990204	AU 1998-88406	19981009
AU 732440	B2	20010426		
HK 1013625	A1	20000420	HK 1998-114978	19981223
AU 9910043	A1	19990304	AU 1999-10043	19990104
GR 3036877	T3	20020131	GR 2001-401740	20011011
US 2003039613	A1	20030227	US 2002-108284	20020326
US 2002150539	A1	20021017	US 2002-113577	20020402
US 2003003055	A1	20030102	US 2002-213600	20020806

PRIORITY APPLN. INFO.:

US 1989-455707	B2	19891222
US 1990-569828	A2	19900820
US 1991-716899	B2	19910618
US 1991-717084	A2	19910618
US 1993-76250	A2	19930611
US 1993-159674	B2	19931130
US 1993-159687	A2	19931130
US 1990-581027	A2	19900911
WO 1990-US7500	W	19901219
US 1991-716793	A	19910618
US 1991-750877	A3	19910826
US 1992-818069	A3	19920108
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US	1995-487230	A3 19950606
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US	1995-485998	A3 19950607
US	1996-665719	A3 19960618
US	1996-741598	A3 19961101
US	1997-796798	A3 19970206
US	1998-118329	A3 19980717

AB Therapeutic delivery systems comprising gaseous precursor-filled liposomes having encapsulated therein a contrast agent or drug are described. Methods of and apparatus for preparing such liposomes and methods for employing such liposomes in therapeutic delivery applications are also disclosed. Dimpalmitoylpyospyhatidylcholine was suspended in normal saline and then extruded five times through 2 μ polycarbonate filters at 800 psi. The resulting liposomes were then dried and added to 1 mL normal saline solution containing 2 μg of DNA on 7000 bp plasmid and filled with N gas. The presence of the gas within the microspheres resulted in much more efficient capture of the ultrasonic energy and release of DNA.

IC ICM A61M005-00
ICS A61B008-00; A61K009-127

NCL 604190000

CC 63-6 (Pharmaceuticals)

IT **Deoxyribonucleic acids**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**complementary**, **antisense**, therapeutic delivery systems comprising gaseous precursor-filled liposomes)

IT **Pharmaceutical dosage forms**
(**liposomes**, therapeutic delivery systems comprising gaseous precursor-filled **liposomes**)

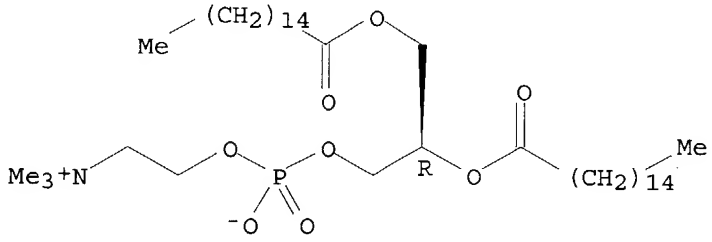
IT **63-89-8**, Dipalmitoylphosphatidylcholine 99-20-7, Trehalose 147-94-4, Cytosine arabinoside 151-21-3, Sodium lauryl sulfate, biological studies 1397-89-3, Amphotericin b 2366-52-1, 1-Fluorobutane **2644-64-6**, 1,2-Dipalmitoylphosphatidylcholine **4539-70-2**, Distearoylphosphatidylcholine 7727-37-9, Nitrogen, biological studies 17966-16-4 25316-40-9, Adriamycin **104162-48-3**, DOTMA 181476-36-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic delivery systems comprising gaseous precursor-filled liposomes)

IT **63-89-8**, Dipalmitoylphosphatidylcholine **2644-64-6**,

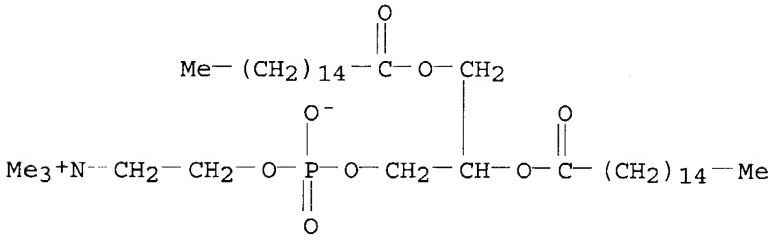
1,2-Dipalmitoylphosphatidylcholine **4539-70-2**,
Distearoylphosphatidylcholine **104162-48-3**, DOTMA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic delivery systems comprising gaseous precursor-filled liposomes)

RN 63-89-8 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

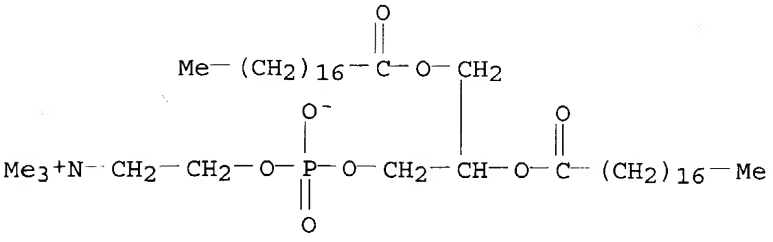
Absolute stereochemistry. Rotation (+).



RN 2644-64-6 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



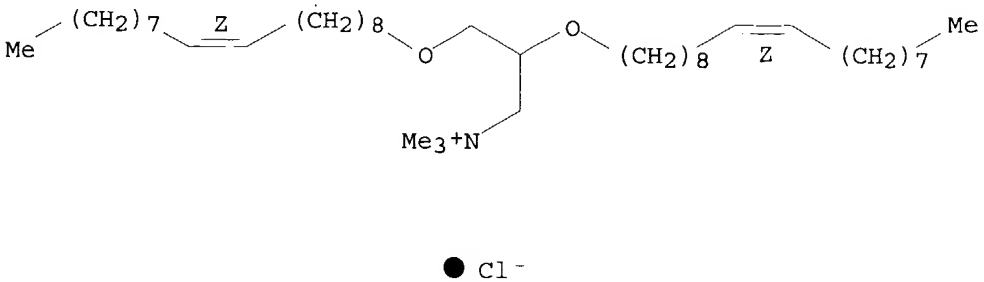
RN 4539-70-2 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 104162-48-3 HCAPLUS

CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L52 ANSWER 59 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:639699 HCAPLUS
DOCUMENT NUMBER: 117:239699
TITLE: Delivery of plasmid DNA into mammalian cell lines using pH-sensitive liposomes: comparison with cationic liposomes
AUTHOR(S): Legendre, Jean Yves; Szoka, Francis C., Jr.
CORPORATE SOURCE: Sch. Pharm., Univ. California, San Francisco, CA, 94143-0446, USA
SOURCE: Pharmaceutical Research (1992), 9(10), 1235-42
CODEN: PHREEB; ISSN: 0724-8741
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We compare the transfection efficiency of plasmid DNA encoding either luciferase or β-galactosidase encapsulated in pH-sensitive liposomes or non-pH-sensitive liposomes or DNA complexes with cationic liposomes composed of dioleoyloxypropyltrimethylammonium-dioleoylphosphatidylethanolamine (1:1, weight/weight) (Lipofectin) and delivered into various mammalian cell lines. Cationic liposomes mediate the highest transient level in all cell lines examined PH-sensitive liposomes, composed of cholesteryl hemisuccinate and dioleoylphosphatidylethanolamine at a 2:1 molar ratio, mediate gene transfer with efficiencies that are 1 to 30% of that obtained with cationic liposomes, while non-pH-sensitive liposomes compns. do not induce any detectable transfection. Cationic liposomes mediate a more rapid uptake of plasmid DNA, to about an 8-fold greater level than that obtained with pH-sensitive liposomes. The higher uptake of DNA mediate by Lipofectin accounts for part of its high transfection efficiency. Treatment of cells with chloroquine, ammonium chloride, or monensin decreases (3-fold) transfection using pH-sensitive liposomes and either has no effect on or enhances cationic liposome-mediated transfection. Therefore plasma membrane fusion is not the only mechanism available to cationic liposomes; in certain cell lines DNA delivery via endocytosis is a possible parallel pathway and could augment the superior transfection efficiency observed with cationic liposomes.

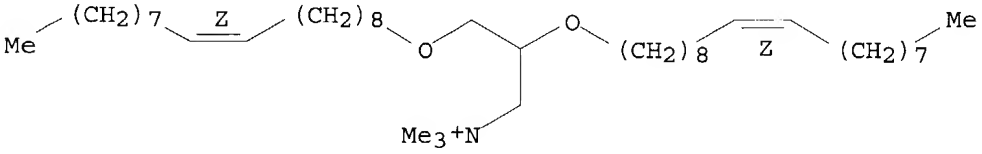
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1

IT **Plasmid and Episome**
(DNA, cationic and pH-sensitive liposomes for delivery of, transfection efficacy in relation to)

IT **Deoxyribonucleic acids**
RL: BIOL (Biological study)
(plasmid, cationic and pH-sensitive liposomes for delivery of, transfection efficacy in relation to)
IT **Pharmaceutical dosage forms**
(**liposomes**, cationic and pH-sensitive, for plasmid DNA delivery)
IT **104162-48-3**
RL: BIOL (Biological study)
(liposomes containing, cationic, transfection efficacy of, in gene therapy)

IT 57-88-5, Cholesterol, biological studies 2462-63-7, Dioleoylphosphatidylethanolamine **68737-67-7**, Dioleoylphosphatidylcholine
RL: BIOL (Biological study)
(liposomes containing, transfection efficacy of, in gene therapy)
IT **104162-48-3**
RL: BIOL (Biological study)
(liposomes containing, cationic, transfection efficacy of, in gene therapy)
RN 104162-48-3 HCAPLUS
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(9Z)-9-octadecenyloxy]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

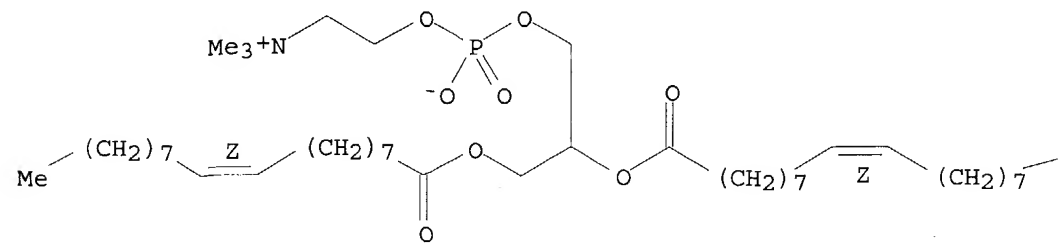


● Cl⁻

IT **68737-67-7**, Dioleoylphosphatidylcholine
RL: BIOL (Biological study)
(liposomes containing, transfection efficacy of, in gene therapy)
RN 68737-67-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacos-18-en-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(9Z)-1-oxo-9-octadecenyl]oxy]-, inner salt, 4-oxide, (18Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



Me